ReFlections

RGA's Global Medical Newsletter

Volume 47, May 2019

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IN THIS ISSUE

FROM THE EDITORS

Greetings! We are pleased to share with you the most recent issue of *ReFlections*.

With this issue we introduce three new writers, each of whom has penned articles focused on expanding our medical understanding of the conditions we deal with on a daily basis.

The first, from Dr. Newman Harris of our Sydney, Australia office, is Part I of a two-part series that outlines the latest ways to define and classify chronic pain as laid out in ICD-11. Understanding how pain informs impairment is an essential piece of our work, and this article provides additional clarity.

The second article, from Sandeepan Basu of our Mumbai, India office, provides an overview of the Fourth Universal Definition of Myocardial Infarction. This well-researched article delves into key aspects of the updated definition, explores its complexity, and presents potential implications for the life insurance industry.

Behavioral economics is an area that is making a substantial splash in many industries and insurance is no exception. We are excited to introduce behavioral economist Matt Battersby, from our London, U.K. office, to our pages. His article, which looks at how behavioral economics can play a role in reducing disclosure gaps, is a fascinating look at how this developing sector of economic thought can optimize how we serve our customers.

A new section is being introduced in this issue which highlights RGA's most recently published thought leadership content with relevance to insurance medicine. We hope you will take a moment to click through to some of these fascinating articles and white papers.

Also featured in this issue is a report about a Grand Rounds at Washington University School of Medicine in St. Louis, presented by Dr. Jeffrey Gordon, one of the world's foremost researchers on the microbiome. The standing-room-only event was sponsored by the **Longer Life Foundation**, the not-for-profit jointly supported by RGA and Washington University School of Medicine in St. Louis, and focused on Dr. Gordon's research into the microbiome and malnutrition in children.

Please enjoy this edition of *ReFlections* and let us know if we can do anything to make it more useful for you.

Thank you,

Peter and Dan

PART I: PROPOSED NEW CLASSIFICATIONS AND NOMENCLATURES FOR CHRONIC PAIN

Abstract

The most recent version of the International Classification of Diseases, 11th Revision (ICD-11), is introducing a new paradigm regarding the classification of pain. This novel approach stratifies pain in ways which are unprecedented and will be new to many readers. It will be critical for insurance medicine professionals to understand these concepts as they will likely impact the assessment of risk and may even affect how claims are assessed and adjudicated.

This is Part I of a two-part article that will explore the new pain nosology. Part I will focus primarily on discussing chronic pain in general as well as chronic primary pain syndromes. Part II will address chronic secondary pain syndromes.

Background

To date, the International Classification of Diseases (ICD) has not provided systematic representation of chronic pain states. The only formal systematic categorization of pain syndromes has been that of the International Association for the Study of Pain (IASP). The most recent (second) edition of that nosology (classification of diseases) was released in 1994 and updated in 2012.[1] A perceived shortfall of appropriate coding was seen as contributing to the inadequacy of evidence-based treatment pathways for persons with persistent pain states.

A new classification system for chronic pain has now been developed by an interdisciplinary task force convened by the IASP in consultation with the World Health Organization (WHO). This new diagnostic system distinguishes chronic primary and chronic secondary pain disorders, integrates existing diagnoses, and claims to provide precise definitions consistent with the content model of the ICD. Released by WHO in June 2018, ICD-11[2] is expected to incorporate this new classification of pain states soon; the decision to do so may be voted on as early as May 2019.

As occurs wherever a new classificatory system is launched, this new nosology is heralded as being "clearly operationalized and easily measurable."[3] Among the stated aims of this new system is the hope that in the future, clinicians and others will be aware that pain can present as the dominant or even sole medical adversity experienced by an individual.

The task force reminds us that while persistent pain may be secondary to an underlying disease process, it frequently persists beyond the normal healing process despite there being no other identifiable explanation. This new classification framework provides a system of suitable diagnoses for pain conditions irrespective of the temporal relationship to other somatic morbidities, be they resolved or ongoing morbidities, or indeed when no associated physical disorder has been identifiable.

Complicating the landscape, a focus of this new nosology is to de-emphasize psychiatric constructs pertaining to somatoform presentations

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Currently, he is based in RGA Australia's Sydney office. He is a Clinical Senior Lecturer at the Pain Management and Research Institute of the University of Sydney. He has also served as a New South Wales branch councillor of the Royal Australian & New Zealand College of Psychiatrists, and remains a panel member of the Medical Tribunal of New South Wales.

and disorders, resulting in some discordance with past and current (2013) versions of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM).

The interdisciplinary task force has provided an overview document[1] and several related co-published articles detailing these proposed diagnoses. In the introduction to their article on Chronic Primary Pain,[4] authors M.K. Nicholas and team indicated dissatisfaction with the definitions and descriptions in the current ICD and DSM, stating that "both have been found wanting in their accounts of chronic pain conditions … neither system reflects the developments in pain research over the last two decades and they do not have clear treatment or management implications."

The German-language version of ICD-10 employed diagnostic language for complex pain presentations which was widely considered most appropriate of all: "chronic pain disorder with somatic and psychological factors."[4] While this language acknowledged potentially equal causal attribution to psyche (mind) and soma (body), concern has been expressed that the chronic pain diagnosis continues to be categorized in the psychiatric section. Appropriately, pointing to advances pertaining to the established science underpinning psychological, social, and central nervous system mechanisms, the authors opined that classifications of chronic pain presentations must accommodate the multiple interacting contributors and set aside considerations of somatic versus psychogenic. They even go so far as to state that a dichotomized consideration such as this has become obsolete given medicine's advancing neuroscientific insights.[4] Such opinions are laudably sophisticated, yet are by no means novel within the psychosomatic medicine fraternity.

Pre-empting the concern that this diagnostic system minimizes or even rejects the potential role which can be played by psychogenesis, Nicholas et al. do acknowledge that "biological changes are closely linked to psychological processes; this is most obvious in neurophysiological brain reactions contributing to changes in pain perception."[4] The reader should appreciate the established knowledge that both pain and mood/anxiety are processed by multiple overlapping parts of the brain's limbic system (i.e., the collected areas pivotal to the regulation of mood, arousal, anger, and impulse), and that this set of shared neuropsychiatric components is widely considered pertinent to aspects of a bi-directional causality apparent in these conditions.

The interdisciplinary panel brought together by the IASP to establish this new classificatory system noted that the novel proposed categories could assist in reducing stigma attached to chronic pain syndromes. To quote: "Because of the success of the behavioral neurosciences, even mental disorders can nowadays no longer be considered purely non-somatic. Of note, all chronic pain, including chronic primary pain, will be coded specifically outside the realms of psychiatric disorders. This accords more with the current scientific understanding of chronic pain and often aligns better with a patient's own views."[2]

As a curious aside, and cognizant again of advances in neuroscience, by the same reasoning one might reasonably suggest that conditions such as schizophrenia and bipolar disorder too cannot be categorized as purely non-somatic; rather, these too are becoming recognized as integrated biopsychosocial phenomena, with increasingly well-defined neuropathological underpinnings. This arbitrary separation of all pain states from familiar historical psychiatric categorizations might warrant some further consideration.

The following is a discussion of the new chronic pain diagnoses and how they are designed to be applied once integrated into ICD-11.

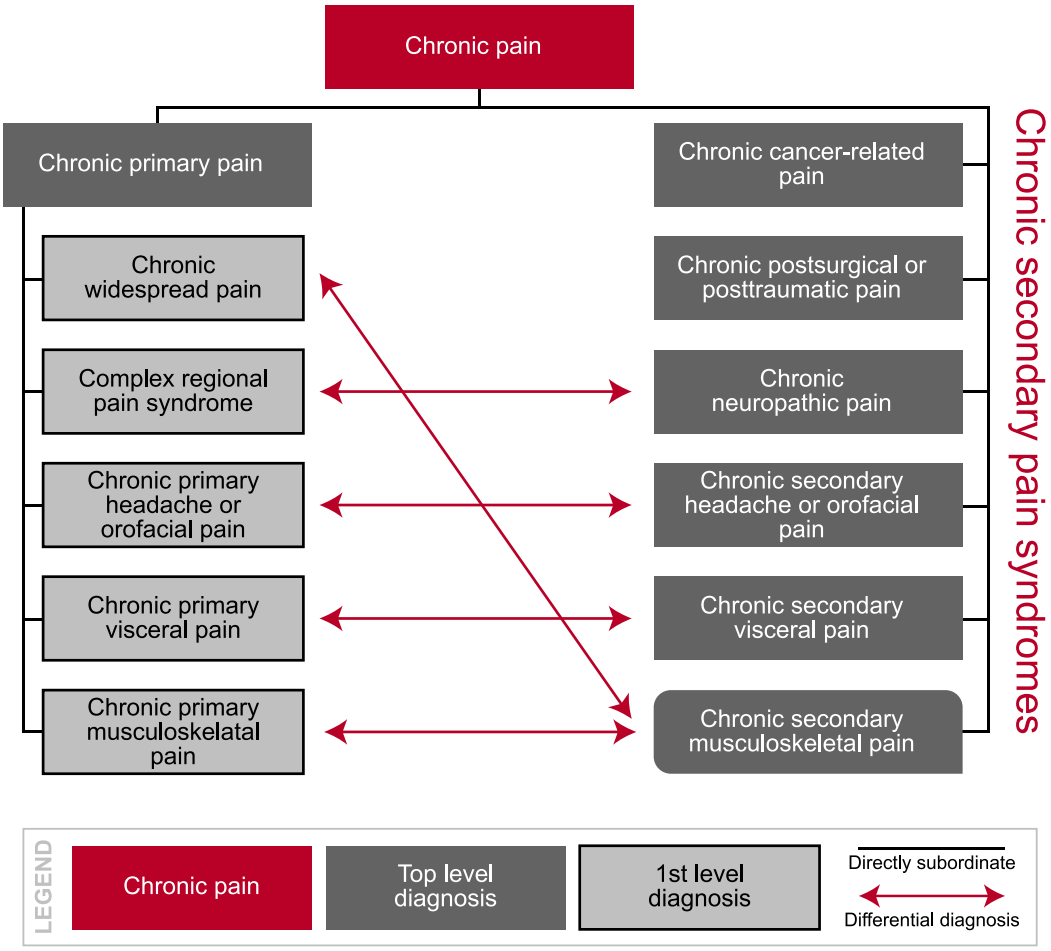
Overview

First, chronic pain is a parent code for seven other top-level diagnostic codes dealing with more common, clinically relevant types of chronic pain conditions:

- chronic primary pain
- chronic cancer-related pain
- chronic postsurgical or post-traumatic pain
- chronic neuropathic pain
- chronic secondary headache or orofacial pain
- chronic secondary visceral pain
- chronic secondary musculoskeletal pain

Figure 1, below, provides a representation of the relationship between this parent code and the above top-level diagnoses, as well as some first-level diagnoses. In chronic primary pain syndromes, as detailed on the left, pain itself is seen as a **disease in its own right**, whereas in chronic secondary pain syndromes, detailed on the right of the diagram, pain initially manifests as a symptom of some other impairment process, such as cancer, accident, nerve damage, or inflammatory disorders.

Figure 1: Hierarchy of Chronic Pain Diagnoses



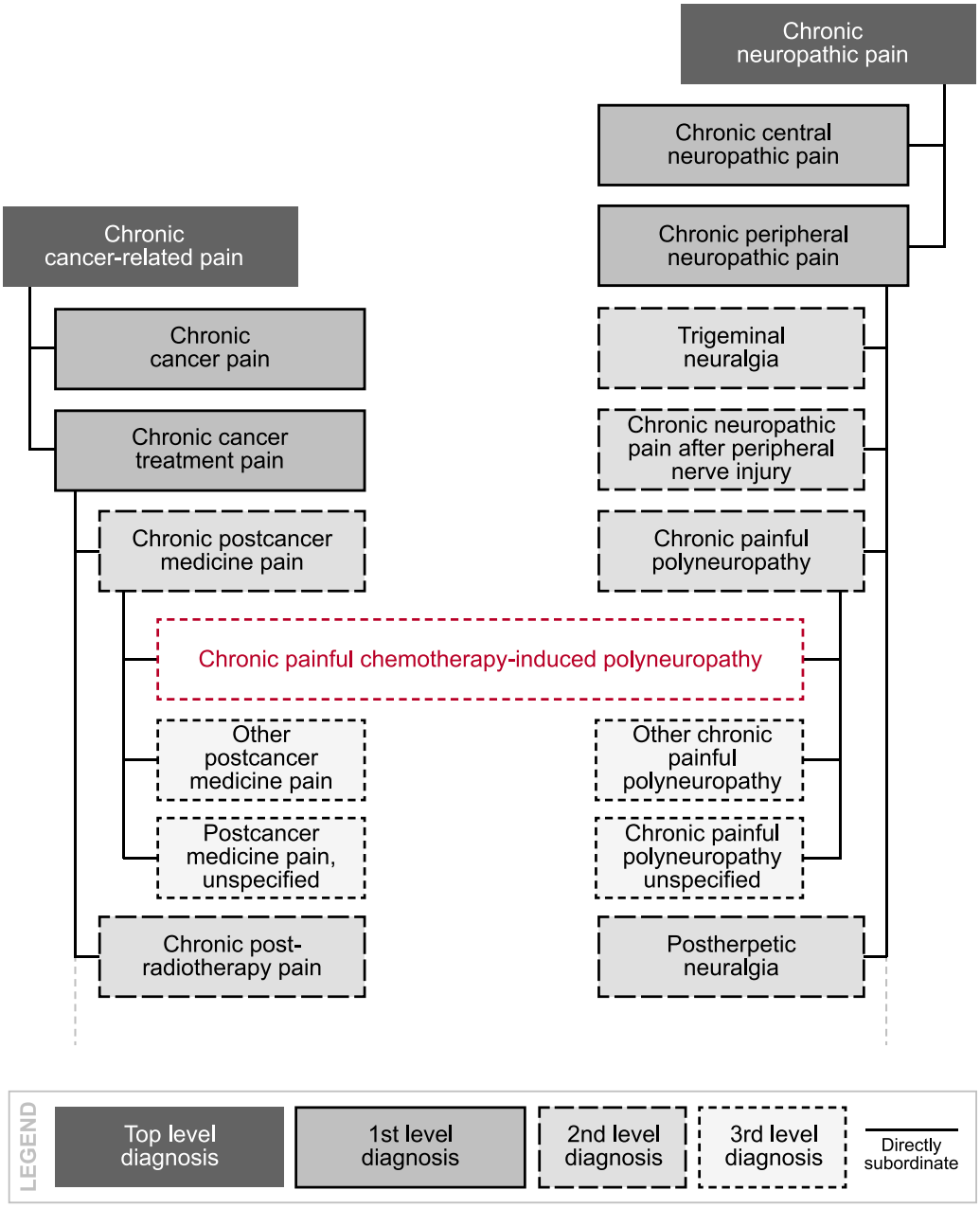
Source: Adapted from Treede RD, et al. Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019 Jan.

A differential diagnosis between primary and secondary pain conditions can sometimes prove challenging. Still, in either case, a person's pain warrants appropriate attention in accordance with the degree of severity and related impairments.

After a spontaneous healing or successful management of an underlying pathological process, persistent pain may sometimes continue and hence the chronic secondary pain diagnosis may remain.

There can be some overlap between these pain conditions; for example, neuropathic pain caused by cancer or its treatment. There can also be overlap between these pain definitions and other disorders in the ICD such as persistent headaches. ICD-11 addresses this by allowing what it calls "multiple parenting," as shown in Figure 2.

Figure 2: Multiple Parenting Construct for Pain



Source: Adapted from Treede RD, et al. Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019 Jan.

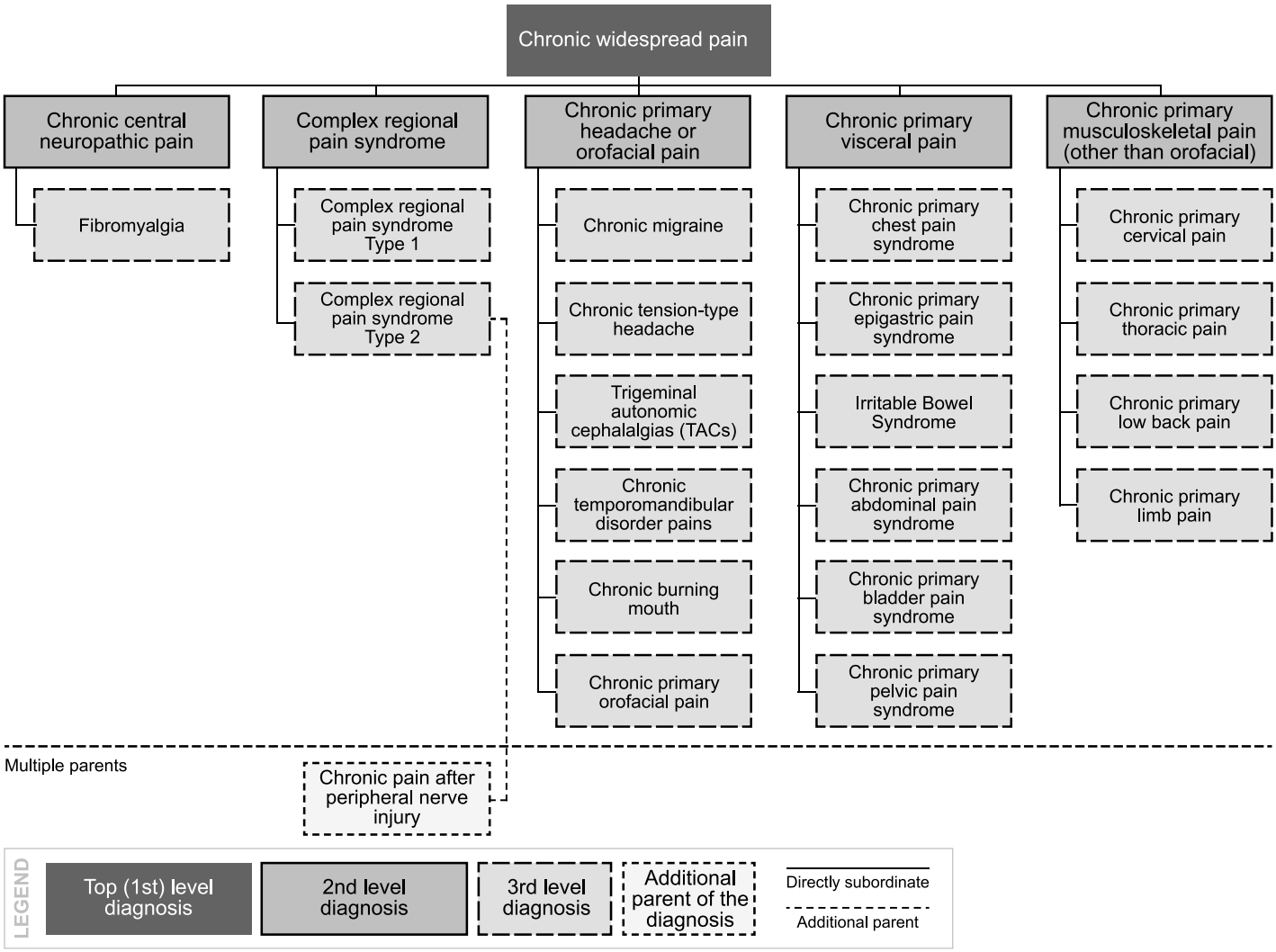
Chronic Primary Pain Syndromes

Chronic primary pain is defined as "pain in one or more anatomical regions that persists or recurs for longer than three months and is associated with significant emotional distress or functional disability (interference with activities of daily life and participation in social roles) and cannot be better accounted for by another chronic pain condition."[2] This is a new category of disorders that apply to chronic pain syndromes not consistent with an identifiable pathology, and so are considered to be best conceptualized as disorders in their own right.

This classification category is specifically designed to detail poorly understood conditions without the application of the former "obscure and potentially laden terms such as somatoform, non-specific, or functional."[4] Some critics have protested that this new category unreasonably de-emphasizes psychiatric processes in such presentations. However, the interdisciplinary task force considered such concerns to be unreasonable and lacking in evidence.

In addition to neuropathic and nociceptive (relating to the perception or sensation of pain) phenomena integral to many primary (and secondary) pain disorders is the recently defined phenomenon of nociplastic pain. Nociplastic pain refers to a neurophysiological mechanism which causes pain to arise because of altered nociception, despite an absence of actual or threatened tissue damage causing neuronal activation, and absent any impact due to identifiable pathology of the somatosensory nervous system.[5]

Figure 3: General Classification Structure of the Hierarchy of Chronic Primary Pain



Source: Nicholas MK, et al. The IASP classification of chronic pain for ICD-11: chronic primary pain. Pain. 2019 Jan.

As indicated in Figure 3, the chronic primary pain classification is subdivided into the following:

- chronic widespread pain (e.g., fibromyalgia)
- complex regional pain syndrome
- chronic primary headache and orofacial pain
- chronic primary visceral pain (e.g., irritable bowel syndrome)
- chronic primary musculoskeletal pain (e.g., non-specific low back pain)

Of course, symptom profiles adequately explained by identifiable pathology discount any of the above primary diagnoses. Chronic secondary pain syndromes must be considered and excluded where possible.

Chronic primary headaches will be cross-referenced, making use of the multiple parenting option of ICD-11. For example, chronic migraine is listed both in the headache session of ICD-11 and the chronic pain section.

Chronic Widespread Pain

Chronic widespread pain (CWP) is a diffuse experience perceived in at least four of the five specified body regions and in at least three or more body quadrants and axial sites. As a primary disorder, the pain is not attributable to an identified nociceptive process in these regions. There will be features consistent with nociplastic pain, such as sensory derangements including spontaneous or excessively evoked pain in the affected regions, and there will be identifiable psychological and social factors contributing to the presentation. Comorbid disturbances will be common as well.

Fibromyalgia syndrome (FMS) is an example of CWP. It is commonly associated with sleep disorders, cognitive dysfunction and other somatic complaints, including irritable bowel syndrome (IBS) and chronic fatigue syndrome.

Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS) has two types – CPRS type I and CPRS type II – and involves pain in a specific region, usually precipitated by trauma. The pain and/or its duration is markedly in excess to that which would be expected. CRPS is characterized additionally by signs and symptoms of autonomic and inflammatory change in the affected part. Symptoms may include hyperalgesia, allodynia (pain resulting from a stimulus which would not normally provoke pain), skin temperature change, perspiration, fluid retention, and altered hair and nail growth. Localized osteoporosis can often ensue. Symptomatology may alter over time, most likely related to nociplastic mechanisms.

In CRPS type I there is no identifiable associated peripheral nerve injury, whereas in CRPS type II identifiable nerve injury is present. (A definition for CRPS can also be found in the ICD-11 section detailing disorders of the autonomic nervous system – another instance of the multiple parenting used in the ICD 11.)

Chronic Primary Headache and Orofacial Pain

These types of pain are defined as conditions that occur on at least 15 days per month and for longer than three months. The duration of symptoms each day is at least two hours when untreated. For many individuals, briefer episodes may occur daily. Other chronic head and orofacial conditions are listed under chronic secondary disorders:

- **Chronic migraine** is defined as in the prior paragraph, provided the presentation of the features are consistent with migraine headache. These include a generally unilateral pulsing pain of moderate to severe intensity. Migraine is commonly exacerbated by physical activity, and may be associated with nausea and/or aversion to light (photophobia) or sound.
- **Chronic tension-type headache** is defined as a frequent episodic headache, typically bilateral, with a pressing or tight quality. While these too may be associated with nausea, photophobia, or sensitivity to sound, they are not usually affected by physical activity.
- **Trigeminal autonomic cephalalgias** (TACs) involves unilateral facial or head pain, usually occurring along with significant local autonomic features such as lacrimation, rhinorrhoea, nasal congestion, and eyelid swelling. This category includes diagnoses of cluster headache and paroxysmal hemicrania.
- **Chronic temporomandibular disorder** (TMD) is one of the most common forms of persistent facial pain. It involves not only the temporomandibular joint (TMJ or jaw hinge) but also the muscles of chewing and related tissues. There are also forms of chronic secondary TMD.

- **Chronic burning mouth** is a distressing disorder which in some people is quite debilitating. Care must be taken to distinguish this from a secondary burning mouth syndrome, which might be attributable to infections or even in some (rare) cases vitamin D deficiency.

Chronic Primary Visceral Pain

Chronic primary visceral pain may be localized to the head or neck, thoracic, abdominal, or pelvic regions. Included in this category may be non-cardiac chest pain, centrally mediated abdominal pain syndrome, IBS, and chronic anal, pelvic, and testicular pain. Notably, a number of disorders formerly termed "functional," psychogenic, or somatoform are now included among chronic primary visceral pain diagnoses and have attracted new names accordingly.

Also included in this diagnostic category is chronic primary bladder pain syndrome, formally termed interstitial cystitis, and chronic primary pelvic pain syndrome.

Chronic Primary Musculoskeletal Pain

The syndromes in this subcategory are labeled according to the site at which symptoms are evident (e.g. non-specific low back pain). These disorders were formally termed "non-specific" in formal nosologies, or attracted vague and imprecise labels in the community.

Conclusion

An understanding of the new and emerging nosology of pain may prove essential for insurance medicine professionals as the terms are adopted in the near future. The understanding will assist in assessing risk and adjudicating claims, as well as providing insight into current biological constructs underpinning the biopsychosocial facets of pain syndromes.

Part II of this article, which will be presented in the next edition of *ReFlections*, will focus on chronic secondary pain syndromes.

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MYOCARDIAL INFARCTION: THE FOURTH FRONTIER

Abstract

Cardiovascular disease (CVD) remains the single largest cause of death globally. According to the World Health Organization (WHO), 31% of all deaths cumulatively can be attributed to CVDs, with myocardial infarction (MI) and stroke accounting for 85% of these deaths.[1] The estimated cost of managing CVD is expected to rise to $1,044 billion by the year 2030.[2] It is thus imperative for insurers to stay current with any updates to the definition of MI, especially, and its consequent impact on claims, underwriting, and product development.

*The **Fourth Definition of Myocardial Infarction**, the most recent update of this important definition, was published in 2018 by a task force consisting of the Joint European Society of Cardiology (ESC), the American College of Cardiology (ACC), the American Heart Association (AHA), and the World Heart Federation (WHF). This article outlines the key aspects of this revision and its potential implications for the life insurance industry, including underwriting guidelines and claims management.*

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Sandeepan Basu is Senior Underwriter – Research and Manual Development at RGA. Based in the Mumbai, India office, his focus is on researching medical advances impacting life insurance and incorporating that information in RGA's Global Underwriting Manual. His experience in life insurance encompasses underwriting, audit, training, and analytics in India, Southeast Asia and the Middle East. Sandeepan earned his Bachelor of Pharmacy degree from Manipal College of Pharmaceutical Sciences, Karnataka, India.

The Evolution of Myocardial Infarction: Understanding and Definitions

The formal definition of myocardial infarction (MI) can be traced back more than 150 years. The timeline in Figure 1 shows the definition's evolution and history, from Rudolf Virchow's description of the cellular basis of venothrombosis in pulmonary embolism, through the 1950s and 1960s – the point at which it was recognized as one of the most common causes of death across Europe and in the Americas.[3]

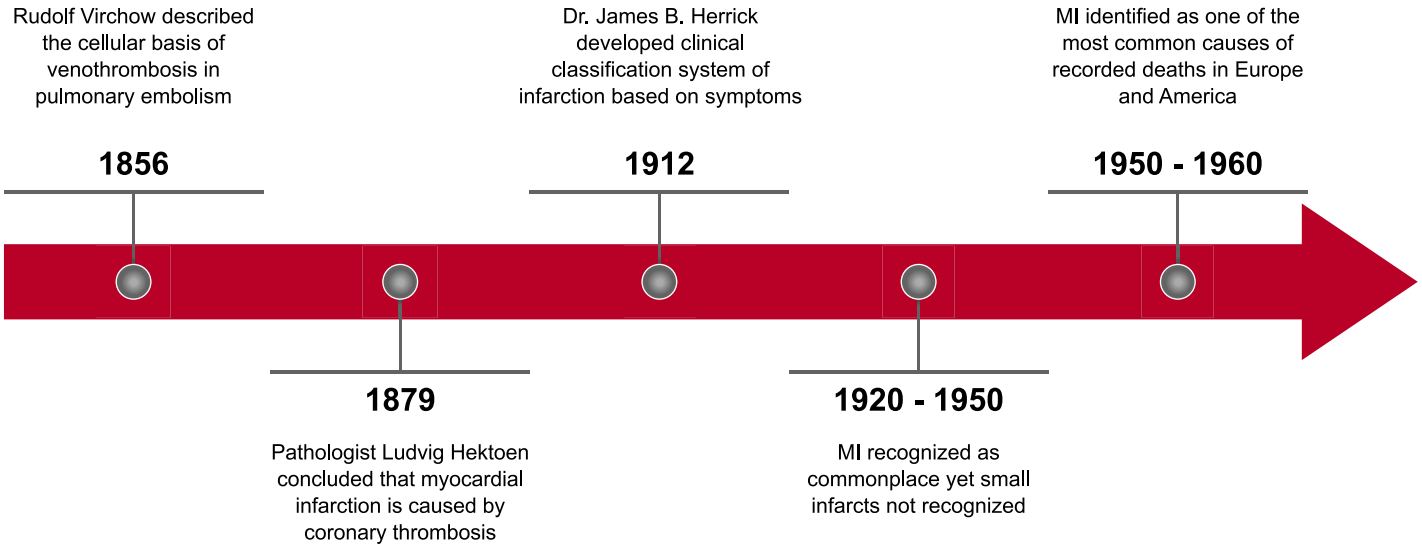


Figure 1: Evolution of MI Definitions – Early Timeline

The MI Definition's Post-1950 Transformation

From the late 1950s to the beginning of the 21st century, the World Health Organization (WHO) has recommended several updates to the definition of MI, resulting in different versions. Initially, definitional language was guided by electrocardiographic-based definitions along with specific symptomatic criteria. However, the discovery in the 1980s of the non-enzyme, cardiac-specific biomarkers known as troponins changed MI's diagnostic criteria completely. By the end of that decade, because of their sensitivity and specificity, the biomarkers troponin T and troponin I had replaced creatine kinase (CK) and creatine kinase-MB (CK-MB) as the preferred biochemical markers for MI, with rises above their normal ranges becoming central to a diagnosis.

Origins of Collaborative and Universal Definitions

In 1971, WHO published a report that established MI as a diagnosis if two of the following three criteria were met:[4, 5]

- Clinical symptoms
- Definite ECG changes
- Increases in cardiac enzymes CK and CK-MB

One of the first collaborative MI definitions was issued in the year 2000, when the European Society of Cardiology (ESC) and the American College of Cardiology (ACC) came together to craft a clinical and biochemical approach of defining MI.

It was not until 2007, however, that the Global MI Task Force (endorsed by the ESC, the ACC, and WHO) introduced what is today known as the modern method of MI classification, better known as Universal Definition of MI.[5, 6]

The 2007 definition's guidelines for diagnosis of MI described the various clinical scenarios in which MI might be diagnosed. The basic notion that myocardial infarction represented myocardial cell death as a result of disruption of blood supply to the heart did not change over time. Five different types of MI, listed in Table 1, were recognized and defined on pathophysiological grounds.

Fourth Universal Definition: Focus on Myocardial Injury

The latest definition of myocardial infarction emphasizes the concept of myocardial injury detected by biomarkers and the importance of defining myocardial infarction only when injury has occurred as a consequence of ischemia. Increasing marker sensitivity for injury has reduced the specificity for infarction and makes it crucial that the clinical circumstances be analyzed in detail.

Acute myocardial infarction is defined as myocardial injury detected by "a rise and/or fall of cardiac troponin with at least one value above the 99th percentile upper reference limit (URL)" which occurs in the setting of acute myocardial ischemia.

It is important to know that myocardial injury can also be a diagnostic entity for other conditions as well. Non-ischemic myocardial injury, for example, may result from other cardiac conditions such as myocarditis or cardiomyopathy, and elevated biomarkers may be found in non-cardiac conditions such as renal failure.[7]

Essentially the revision of MI definitions not only has an effect on the traditional clinical definitions for the various types of MI but also a secondary effect on other associated cardiovascular disorders such as MI with non-obstructive coronary arteries (MINOCA) and Takotsubo syndrome.

MI Definitions and Subtypes: Comparing Key Differentiators

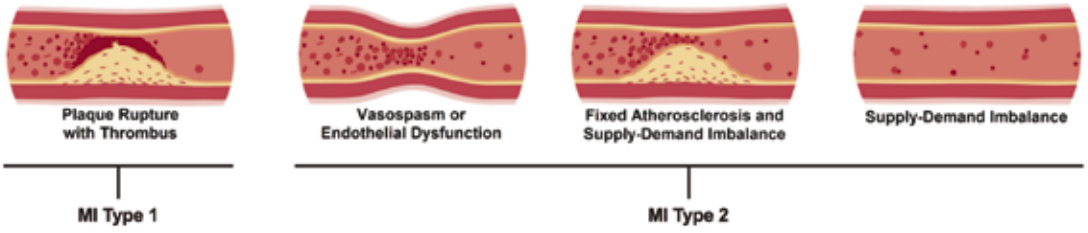
The detailed evidence used in the latest definition to define the different types of MI remain similar to those in preceding definitions.[7] Table 1 (below) provides a general overview.

Table 1: Types of Myocardial Infarction

Type 1	Classical MI. Acute atherothrombosis, caused by coronary artery disease (CAD) with plaque rupture and thrombus formation.
Type 2	Caused by a rising imbalance between myocardial oxygen supply and demand in absence of coronary plaque rupture with thrombosis. Type 2 infarction may occur in the context of normal coronary arteries. Varying degrees of obstructive coronary artery disease may accompany this entity and contribute to the supply and demand imbalance.
Type 3	Denotes patients suffering from cardiac death before evidence of cardiac biomarker elevation could be made available and with presumed newfound ECG changes.
Type 4 and Type 5	These are infarctions arising as a consequence of coronary procedures such as percutaneous coronary intervention (PCI) (Type 4) and coronary artery bypass grafting (CABG) (Type 5). Type 4a infarction is diagnosed if an infarct is caused during the routine deployment of a stent for a coronary occlusion. Type 4b infarction is diagnosed when a previously deployed coronary stent acutely thromboses with the abrupt cessation of blood flow. Type 5 infarction is defined if a myocardial infarction occurs during surgical coronary artery bypass grafting.

It is often difficult to differentiate Type 1 from Type 2 MI (Figure 2). A diagnosis of Type 1 MI may be made upon the identification of a coronary thrombosis and a ruptured plaque by angiography including intracoronary imaging. A diagnosis of Type 2 infarction requires evidence of an imbalance between myocardial oxygen supply and demand which is unrelated to coronary thrombosis even if an angiogram happens to demonstrate coronary disease.

Figure 2: Key Differences between Type 1 & Type 2 MI



The Curious Case of Biomarkers: Cardiac Troponins

Troponin is the biomarker of choice for the detection of any form of cardiac injury. Cardiac-specific troponins troponin I (cTnI) and troponin T (cTnT) are known to be highly sensitive markers for the evaluation and diagnosis of myocardial injury and subsequent MI.

The troponin complex in heart muscle cells comprises three specific sub-units (troponin I, T and C). Troponin I and troponin T are considered cardio-specific while troponin C occurs in other muscle tissue.[8]

The 99th percentile, which has been defined as the cutoff value for troponin elevations for diagnosing MI, is quoted by the various assay manufacturers for all assays. Some laboratories may report age- or gender-specific troponin reference ranges.[9]

While an MI can only be diagnosed on biomarker grounds when a level exceeds the 99th percentile for a reference population, there is also a requirement that the level be in flux. A rise and/or fall must be identified to avoid false diagnoses in those with medical conditions associated with chronically elevated troponins. The magnitude of change that reflects a true rise or fall depends on assay characteristics, but is usually defined as a change of 20% to 50%.

Type 4a and Type 5 myocardial infarctions require specific orders of magnitude of troponin above the 99th percentile to be exceeded.

If cTn data is unavailable, the cardiac enzyme CK-MB serves as the best alternative marker.

Although there is no question as to the importance of cardiac troponins in the diagnosis of MI, there are a few points to ponder which do not yet have firm conclusions:[7]

- There is no absolute consensus about the specific criteria to define the 99th percentile URL.
- Although age-dependent assays are not currently mandated or recommended, variability of assay results for individuals age 60+ years or with comorbidities cannot be ruled out.
- The use of gender-specific 99th percentiles is not currently mandated but should be used if provided. Lower values are observed in women compared to men.

Despite the very high sensitivity of the troponin assays already in use, it is possible that even more sensitive assays might be developed to detect myocardial injury, which would likely result in increased MI incidence rates. MI incidence rates could also be affected by assay sensitivity for myocardial necrosis, which may be indicative of false positive MI diagnoses. As the latest high-sensitivity assays are able to detect very small levels of troponin elevation, it is no longer possible to directly equate detectable troponin rises with MI.

Interpretation of an elevated troponin level requires careful consideration of the clinical context. The increased sensitivity for the detection of an elevated troponin will be associated with some loss of specificity for MI since myocardial cell death can occur in many situations other than ischemic infarction.

Understanding Non-MI Troponin Elevations

In cases where troponin elevation occurs without clear associations, such as ECG changes and/or imaging or angiographic findings of acute myocardial ischemia, it could be a result of myocardial injury due to causes other than MI, and could be of cardiac or systemic origin (Figure 3).

Another familiar and common but misleading assumption is that rising and falling troponin patterns only occur in the context of MI. That too needs to be substantiated in context with all other findings as described under the Fourth Universal Definition to confirm MI.[7]

It is important to understand that the current definition utilizes the terminology “myocardial injury without infarction” from a pathophysiological perspective. However, it may not be that straightforward from a clinical point of view. Clinicians need to evaluate all possibilities before concluding whether a troponin elevation is due to MI or non-MI conditions.

Imaging Techniques and Diagnostic Testing

Five types of imaging tests are the tests of choice to diagnose MI and related CVDs: echocardiography, radionuclide imaging, single photo emission computed tomography (SPECT), cardiac magnetic resonance imaging (CMRI), and computed tomographic coronary angiography (CTCA).

While echocardiography would help to differentiate non-coronary pathologies known to cause chest pain (e.g., hypertrophic cardiomyopathy), CMRI can help distinguish acute from chronic myocardial injury. CTCA may be used to diagnose coronary artery disease (CAD) in patients with acute coronary syndrome (ACS), and it can also be helpful for acute MI detection. [7]

Figure 3:
Myocardial Injury for MI- and Non-MI-Related Factors

Reasons for Elevation of Cardiac Troponin Values Due to Myocardial Injury
Myocardial injury related to acute myocardial ischemia
Atherosclerotic plaque disruption with thrombosis
Myocardial injury related to acute myocardial ischemia because of oxygen supply/imbalance
Reduced myocardial perfusion; e.g.: • Coronary artery spasm, microvascular dysfunction • Coronary embolism • Coronary artery dissection • Sustained bradyarrhythmia • Hypotension or shock • Respiratory failure • Severe anemia **Increased myocardial oxygen demand; e.g.:** • Sustained tachyarrythmia • Severe hypertension with/without left ventricular hypertrophy
Other causes of myocardial injury
Cardiac conditions; e.g.: • Heart failure • Myocarditis • Cardiomyopathy (any type) • Takotsubo syndrome • Coronary revascularization procedure • Catheter ablation • Defibrillator shocks • Cardiac contusion **Systemic conditions; e.g.:** • Sepsis • Chronic kidney disease • Stroke, subarachnoid hemorrhage • Pulmonary embolism, pulmonary hypertension • Infiltrative diseases; e.g., amyloidosis, sarcoidosis • Chemotherapeutic agents • Critically ill patients • Strenuous exercise

Source: Adapted from Thygesen K, et al. Fourth universal definition of myocardial infarction. 2018.

The Insurance Paradox

The evolution of the MI definition over the years has been intriguing. With CVD accounting for 31% of deaths globally and MI being one its chief components, these impairments pose a great challenge to the insurance industry. The impact on various critical illness and cardiac-specific products, as well as on the management of definitions for the covered/exempt conditions defined within each, is most profound.

What are the implications of this latest revision for the insurance industry?

MI Definitions and Subtypes

"Myocardial injury" and its related concepts must be correctly understood, as it is an integral part of the approved definition of MI.

- **Type 1 MI:** Fundamentally unchanged from its previous definitions. The only aspects of the definition that may need standardizing are the associated evidence items needed to confirm it.
- **Type 2 MI:** Type 2 represents one of the pivotal and most challenging talking points of the current updated definition. That acute atherothrombotic plaque is not a prerequisite and instead a sustained tachyarrhythmia with clinical manifestation of MI that could lead to myocardial injury and consequently to Type 2 MI remains a bit of an enigma. The thin line between cardiac injury and infarction may appear to be blurred in patients who are unstable, unconscious, hypoxic, or are mechanically ventilated in the ICU. Furthermore, establishing Type 2 MI is a challenge in itself, given that the rise and fall of troponin values resembles those of other CVDs.

  Going forward, Type 2 MI might be seen more frequently as a claimed event under MI. Thus it is important that pricing, underwriting, and claims have a uniform understanding of it and work in cohesion to build guidelines around it.
- **Type 3 MI:** This type of MI has not historically proven to be of significant challenge to the insurance industry as standard CI definitions require a survival period.
- **Types 4 and 5 MI:** Myocardial injury due to coronary procedures is different from ischemia and more prevalent than generally believed. Nearly 32% of patients have procedural myocardial injury after PCI or coronary artery bypass grafting (CABG), but

this injury is not necessarily definable as MI.[7] The arbitrary order of magnitude of troponin elevation that has been proposed for the purposes of defining procedural MI has limited this as a diagnosis.

The concept of procedural myocardial injury as opposed to procedural infarction must be distinguished for and priced accordingly. Insurance- or product-specific definitions need to recognize this aspect and specify their inclusion or exclusion according to features and pricing considerations. Careful consideration and clear, unambiguous guidelines would help streamline this aspect.

MINOCA and Takotsubo Syndrome

A few cardiovascular disorders deserve special mention, either for being new additions to the Universal Definition or for their proximity to MI clinically and ability to exhibit MI-like features. It is extremely important that insurers have a detailed understanding of these disorders in order to take appropriate courses of action for underwriting and claims purposes.

- **Myocardial infarction with non-obstructive coronary arteries (MINOCA):** As the name suggests, this condition fits the Universal Definition of acute MI, yet is identified as having non-obstructive CAD (absence of stenosis $\geq$ 50%) and no clinically specific cause for acute presentation at time of angiography. MINOCA is present in 6% to 8% of the MI cohort population and is common among females and non-ST segment elevation MI (NSTEMI) patients. Although generally there is a series of disruptions or a dysfunction of a coronary artery (plaque, akin to Type 1 MI) or a coronary spasm leading to MINOCA, it should not be confused with other myocardial disorders such as myocarditis, Takotsubo syndrome, and other cardiomyopathies which are categorized under troponin-positive, non-obstructive coronary artery syndromes.[10]

  To summarize, high troponin levels and normal or non-obstructive coronaries are key indicators of MINOCA. As MINOCA is a relatively newly identified condition with subtle overlaps with other cardiovascular disorders, it would require sophisticated risk assessment and experienced understanding to determine its qualification as MI, as age and gender also play a crucial role. However, the need, at least from a claims perspective, is to focus on the detailed reasoning by the attending cardiologist to ensure the diagnosis of MINOCA as MI.

- **Takotsubo syndrome (TTS)** is another relatively newly defined cardiovascular disorder. With a staggering 90% of cases occurring among post-menopausal women and triggered generally by stress or physical factors, it shows a remarkable similarity to ACS. Inpatient mortality coincides with that of ST-segment elevation MI (STEMI) (4% to 5%). While the ECG changes may be similar in MI and TTS, the ECG changes in TTS are usually not in definable coronary vascular territories.

  The rise and fall of troponin levels is indicative of myocardial injury. CAD is present in 15% of TTS cases, which makes the situation more complicated.[7]

  TTS is not considered a part of MI definition despite the fact that some of these will have coronary disease. Although there are some clinical similarities between TTS and both MI and cardiomyopathy, it would be prudent for insurers to treat TTS and MI as individual entities.

Troponin Elevation and Diagnostic Tests

- **Troponin factor:** A recent article recommends obtaining serial cTn values and comparing them across different intervals for the assays to be reported. However, in reality it is unlikely that underwriters receive a complete set of comprehensive information.[8] The article does emphasize obtaining gender-specific 99th percentiles, if available, as bias may prevent underdiagnoses in women and overdiagnoses in men, but does not mandate it. With differential points suggested for evaluation, this opens up a new Pandora's box in terms of the availability of such tests as well as implications on pricing assumptions. It will definitely have an effect on the current percentage distribution (e.g., gender bias) of a cohort qualifying for MI. Insurers should monitor this closely across geographies and have a focused discussion in order to develop a uniform approach. As of now, insurers depend on hospital or clinic assays, their respective limit ranges, aggregate or gender-specific, to confirm diagnosis of MI and trigger the corresponding claim.
- **Diagnostic tests:** There is no significant change from a diagnostic perspective from the preceding definitions (ECG changes are only required for diagnosis of MI), but when evaluating a claim from an insurance risk assessment perspective, it is recommended to review more advanced diagnostic

tests, if available, to avoid any overlap with other CVDs. Thus, advanced tests such as CMRI or CTCA may become more commonly encountered.

Final Word

The Fourth Universal Definition of Myocardial Infarction, while providing more clarity for the insurance industry, is designed for clinical purposes. The concept of myocardial injury, the varying elevations of troponins related to myocardial injury or otherwise, and the newly associated or related CVDs which may overlap with MI, are well documented. However, the implications of these new definitional factors on the insurance industry are currently less conclusive than might have been anticipated.

Age, gender, and clinical diagnosis, including all related tests (including but not limited to cardiac biomarkers and advanced imaging techniques), must be carefully considered before drawing any final conclusions on a firm diagnosis of MI, as both the psychological and legal implications are profound. Any doubts or suspicion of other cardiovascular disease overlap must be overruled by conducting tests with higher specificity for the same. In countries with limited availability of troponin or imaging techniques, the challenge is more acute and product pricing will vary accordingly.

Furthermore, consideration of the new Universal Definition of MI does raise the question that an update of this magnitude might impact all insurance industry verticals, including costs and global revenues. Is now the right time to collaborate as an industry and form standardized guidelines of inclusion and exclusion, which might help mitigate ambiguity and provide consumer-friendly coverage? RF

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BEHAVIORAL ECONOMICS, DISCLOSURE GAPS, AND CUSTOMER JOURNEYS

Abstract

Few industries are as reliant on customer honesty as is life and health insurance. The use of new data sources to assess mortality and morbidity risk will undoubtedly change how we price and underwrite business in the future, but for now we are still quite dependent on applicant disclosures.

We would like to think people are completely honest and accurate when applying for insurance, but this is often not the case. This can lead to miscalculated and mispriced risk for insurers, and for consumers, it can mean higher average premiums and invalidated policies.

Fortunately, solutions exist that can reduce the disclosure gap. RGA's Behavioral Science team has recently been conducting randomized control trials involving more than 20,000 individuals from 10 markets (Australia, Canada, France, Hong Kong, India, Malaysia, Singapore, South Africa, U.K., and U.S). The results highlight simple and practical steps insurers can take to improve disclosures and customer journeys.

Understanding Disclosure Gaps

Legendary advertising genius David Ogilvy once said: "Consumers don't think how they feel. They don't say what they think and they don't do what they say." Clearly, he understood disclosure gaps!

This sentiment applies quite easily to insurance applicants as well, as there is a consistent gap between what they say they have, are, and do, and what is indicated by population averages. Research by the medical testing and diagnostics company ExamOne, for example, shows that 18.2% of U.S. life insurance applicants fail to declare they are obese or morbidly obese,[1] and 22.9% of applicants do not honestly disclose the extent of their tobacco usage.[2]

There are many reasons for disclosure gaps. Inaccuracy on behalf of the applicant may be intentional, driven by financial motives such as a desire to ensure coverage and reduce premiums, or by psychological motives such as the desire not to admit problematic things to oneself or others. Unintentional inaccuracy, also a factor, can be driven by not understanding the question or a lack of knowledge of one's behaviors, but it can also be influenced by motives such as the applicant's desire to use minimal mental effort when answering questions. Understanding these varied motives may enable our industry to address their effects.

Behavioral science has shown that the way a question is phrased and the context in which it is asked can significantly impact the accuracy of the responses it elicits. Over the past year, RGA's Behavioral Science team has been conducting multiple trials and experiments to determine how best to design health questions in policy applications so that they elicit the most accurate responses.

In our latest research, participants – 2,000 from each of 10 markets – were asked to complete a healthy living survey. Participants were

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Matt Battersby is Vice President and Chief Behavioural Scientist at RGA. Based in RGA's London (U.K.) office, he is responsible for the effective development and deployment of behavioural science-informed models to RGA and to its clients for use in underwriting, claims, risk management and customer engagement. Matt has a Master of Science (MSc) in Behavioural Science from the London School of Economics and a Bachelor of Science (BSc) in Economics and Philosophy from the University of Bristol.

provided with a financial incentive to complete the survey, and to replicate the financial incentive that exists in the context of insurance policy applications to be less than completely honest, were told they would qualify for additional incentives if they were considered healthy.

We tested multiple versions of application questions in the following disclosure categories:

- Alcohol consumption
- Drug usage
- Tobacco usage
- Prior and existing medical conditions
- Family history of prior and existing medical conditions
- Height and weight

One version of each question, considered the control version, was based on current standard practice across the life insurance industry. To create control version questions, applications forms from 15 insurers were analyzed. The applications were for fully underwritten, simplified issue, and final expense products.

Respondents were presented with one randomly determined version of each question. Running the experiment as a randomized control trial meant relative disclosure rates could be compared in response to each version of each question. All results presented below were significant at the 99.9% confidence level ($P<0.001$).

Closing the Disclosure Gap

Past RGA research suggests there are three key principles for increasing the accuracy of applicant disclosures: Make it easier to be accurate, easier to be truthful, and harder to lie – that is, to make a false statement with the specific intent of deceiving. Our most recent experiment tested and proved simple yet effective ways to put these principles into practice.

Make it easier to be accurate: The key to making questions easier to answer accurately is to reduce the amount of mental processing and working memory required, known as "cognitive load," needed to do so. In the drive to simplify applications by reducing the number of questions, insurers often combine multiple questions into one, thereby increasing the cognitive load required to answer each one. Applicants tend to want to answer questions quickly, and will often use mental shortcuts instead of giving full thought and time.

Ways to minimize cognitive load needs for applicants include:

- Using simple, everyday language – leave no room for confusion or ambiguity.
- Avoiding asking more than one thing in a question – numerous simple questions are easier to process than one long question.
- Prompting memory by listing possible answers – provide lists of common alcoholic drinks, drugs, medications, and other possible options.
- Avoiding free-text responses wherever possible – drop-down menus, scales, and other methods can provide for a range of responses.

Thus far, RGA's behavioral science team research is showing that these methods work particularly well for questions on personal and family medical histories. For example,

family history questions typically ask applicants to think simultaneously about each family member and all relevant medical conditions. We tested this standard format versus first asking how many siblings the applicant has and then asking them to go through the medical disclosure for each family member one by one. This approach increased the number of applicants from 51% to 62% who disclosed that at least one family member had at least one condition.

Importantly, this alternative question style had no significant impact on the time taken to complete the family history segment of the questionnaire. This emphasizes that fewer questions do not necessarily mean a simpler application process. An applicant will find it quicker to answer a questionnaire and to be more accurate when presented with a greater number of simpler questions.

Make it easier to be honest: Often people do not want to admit to their behaviors if there is shame or social stigma attached. They would rather shade the truth, or even be outright untruthful, than cause themselves psychological pain. Insurers therefore need to design questions in ways that let applicants feel comfortable that their behavior is acceptable and normal.

Ways to phrase questions that can normalize and destigmatize applicant answers include:

- Assuming the behavior exists – ask "when did you last...?" rather than "have you ever...?"
- Minimizing an applicant's feeling of being at the extremes of acceptable norms – provide multiple answer options that are weighted towards extremes of behavior.

Questions with the most potential to elicit feelings of shame or stigma are those asking about alcohol, tobacco, drug use, and weight.

In the drive for simplicity, many insurers have moved to asking simple binary questions, such as: "Do you smoke? Yes/No." "Do you drink more than 28 units a week? Yes/No."

A problem with binary questions such as these is that they make the underwriting rule, and therefore the "wrong" answer, too obvious. In addition, they increase the psychological cost of being honest: For example, someone who smokes three cigarettes a day might not consider themselves a smoker, but having to tick the "smoker" box on their application means admitting to themselves that they are.

Figure 1 shows how we tested replacing standard binary "Have you ever used...?" style questions for tobacco and drugs with "When was the last time you used…?"

Figure 1: Tobacco — Assume the behavior

When was the last time you used any of the following tobacco or nicotine substitutes?

Cigarettes						
In the past month	In the past 6 months	In the past 12 months	1-5 years ago	6-10 years ago	More than 10 years ago	Never

How frequently do you use, or did you use…?

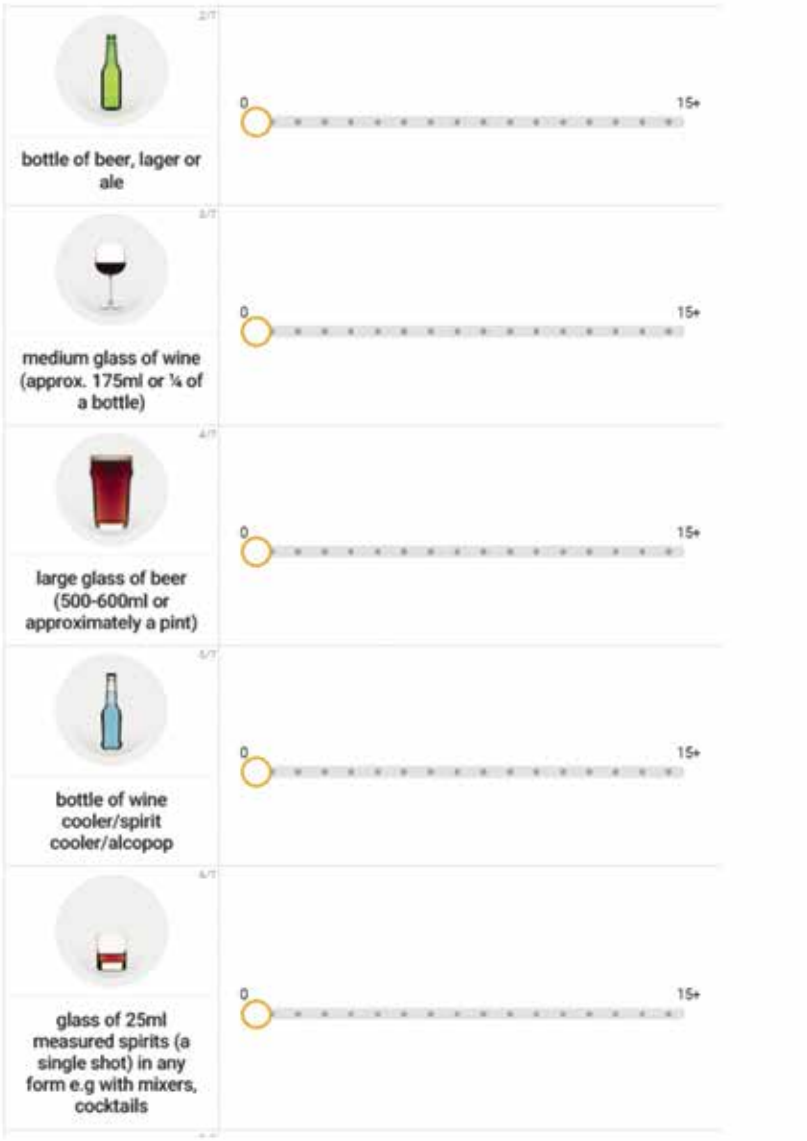
Cigarettes							
40 or more per day	30 or more per day	20-29 per day	10-19 per day	1-9 per day	Less than 7 per week	Less than once a week	Less than once a month

questions. We then provided multiple answer options weighted towards most recent and most frequent usage. Applying these principles increased disclosure of tobacco use from 35% to 52%, disclosure of all drug use from 10% to 18%, and disclosure of marijuana use from 8% to 19%. This question format also had a particularly high impact on drug use disclosure in markets such as Hong Kong, Malaysia, and Singapore, where drugs laws are strictly enforced and where higher stigma is attached to their usage.

We applied the same principles to the alcohol disclosure question but also tested additional changes. Figure 2 shows how to destigmatize high alcohol consumption. We provided high-value scales rather than free-text responses, which increased average disclosure rates from 3 to 8 drinks per week.

This question also shows how memory prompts were used to make it easier to be accurate. Disclosure was strongest when both techniques were used.

Figure 2: Alcohol — Normalize excessive behavior



Make it harder to lie

No one is completely honest all the time. Most people tend to shade or stretch the truth, or even outright lie, up to the level that maintains their self-image as reasonably honest individuals. This is possible when it is easy to do so and easy to self-justify having done so.

Ways to make it harder to lie and let the applicant self-justify include:

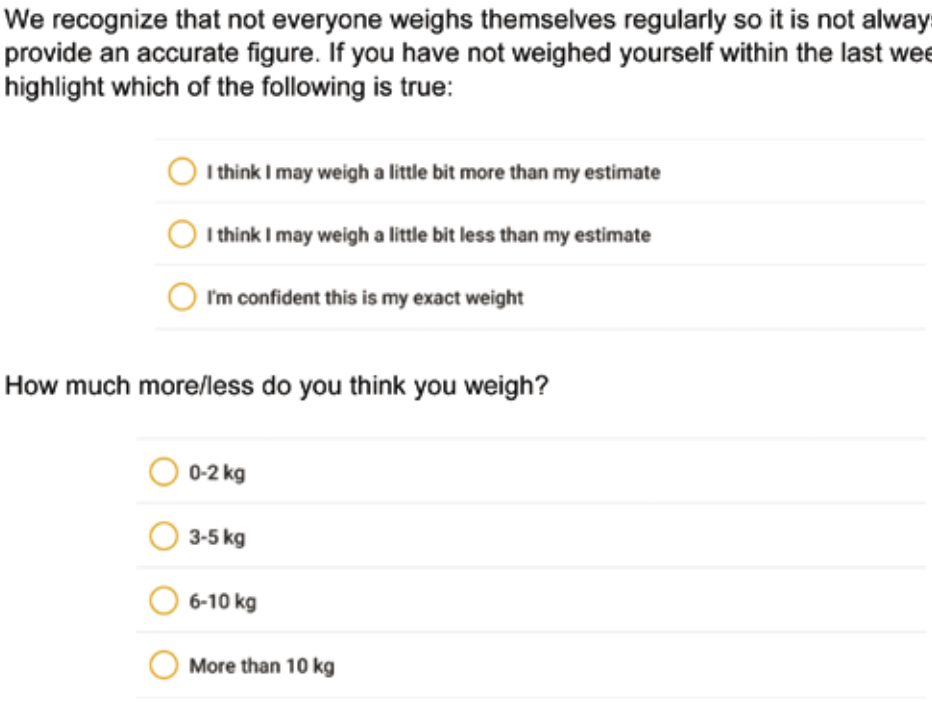
- Not making the "wrong" answer obvious – avoid binary questions and clear cut-off points.
- Increasing the applicant's sense that answers are being monitored (sentinel effect) and the salience of their decision to lie – ask for double-confirmation.
- Making lying more psychologically jarring by using language that triggers an emotional response.

We tested the principle of asking for double-confirmation in the weight question and in asking for a commitment to honesty at the start of the survey.

Previous research has suggested that asking applicants to confirm they will answer a questionnaire honestly and accurately, usually by ticking a box, before answering questions can increase disclosure rates. We tested different versions of these so-called "honesty statements" and found that asking for a double-confirmation increased subsequent disclosure by 5%.

One of the simplest questions might seem to be that of height and weight, but it has proven to be surprisingly difficult for many to answer accurately. Partly, it is a knowledge problem, as people generally do not measure or weigh themselves frequently. Many know or at least suspect that they weigh more or less than they should and are embarrassed to admit it, or think the chances of their inaccuracy being found out are small. Figure 3 shows the double-confirmation question that came after the initial height and weight question. It was designed to show empathy with the applicant and make untruthfulness more conspicuous, and so trigger the sentinel effect.

Figure 3: Weight — double confirmation



When asked this question, 31% of respondents disclosed that they likely weighed more than the answer they had just given and 16% indicated they likely weighed less. For those who weighed more, the average estimate of how much more they weighed increased the BMI value by 1.2.

Conclusion: Honesty is the Best Policy

This latest research shows that simple changes in the way application questions are phrased can increase disclosure significantly. This clearly has benefits for insurers and reinsurers, as more accurate responses can improve underwriting and pricing decisions. It also has clear benefits for the applicants themselves, as more accurate and personalized risk assessments can reduce premiums for those who may previously have found themselves categorized alongside poorer risks.

Over the next 12 months, RGA will continue to conduct research to determine the best ways to ask questions and structure an application form. It is clear that simply rephrasing questions so that is easier for applicants to respond accurately and honestly can make a significant difference. This is the low-hanging fruit that we can all easily reach. Unfortunately, these techniques are unlikely to change the behavior of those who are determined to misrepresent themselves. RGA is exploring other ways to address this problem.

In addition, we will focus not just on how a question is asked, but by whom. Our research to date has focused on direct-to-consumer application disclosures but often there is an intermediary in the process, and the role of the messenger can often outweigh that of the message. For example, a financial adviser could alter the impact of these strategies as insurers must rely on how these advisers communicate the questions. We are also testing the influence of different messengers and the relative merits of online, face-to-face, telephone, and artificial intelligence.

Better questions can also improve customer journeys, making it simpler and quicker to apply for cover. As our research has highlighted, creating questions that are easy to answer is more important than simply trying to decrease the number of questions. More and clearer questions can increase accuracy without increasing the time to answer. When it comes to cognitive load, sometimes less really is more.

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Longer Life Foundation

An RGA/Washington University Partnership

LONGER LIFE FOUNDATION SPONSORS INTERNAL MEDICINE GRAND ROUNDS

Jeffrey Gordon, M.D., one of the giants worldwide in the fields of microbiology and immunology, attracted a standing-room-only crowd for his Grand Rounds talk on January 17, 2019 at Washington University School of Medicine in St. Louis, entitled: "Development of microbiota-directed complementary foods for treating childhood undernutrition."

In his presentation, Dr. Gordon, known as "father of the microbiome," discussed how understanding the microbiome is key to understanding intestinal function, and how, in his research, it is becoming clear that this understanding has the potential to enhance both diagnosis and treatment of childhood-age severe acute malnutrition (SAM), especially in areas of the world where SAM is a frequent occurrence.

Standing (left to right): Dr. Daniel D. Zimmerman, Managing Director, Longer Life Foundation and Senior Vice President, Chief Medical Director, GST, RGA; Dr. David Perlmutter, Dean of the School of Medicine, Washington University in St. Louis; Dr. William A. Peck, Retired Executive Vice Chancellor for Medical Affairs and Retired Dean of the School of Medicine, Washington University in St. Louis; and Dr. Jeffrey Gordon, Chairman of the Department of Pathology & Immunology, School of Medicine, Washington University in St. Louis.

This Grand Rounds, sponsored by the **Longer Life Foundation**, commemorated the 20th anniversary of the foundation, a partnership between RGA and Washington University School of Medicine in St. Louis that supports groundbreaking research into topics related to human longevity, health, and wellness.

Dr. Daniel D. Zimmerman, Managing Director of the **Longer Life Foundation** and Chief Medical Director, RGA Global Support Team, opened the Grand Rounds, provided the audience some background on the **Longer Life Foundation**, and then introduced Dr. David Perlmutter.

In his introduction to Dr. Gordon's talk, Dr. David Perlmutter, Dean of the School of Medicine and a vice-chair and board member of the **Longer Life Foundation**, outlined Dr. Gordon's distinguished professional accomplishments – he is Chairman of the Department of Pathology & Immunology as well as Director of the Edison Family Center for Genome Sciences & Systems Biology – and his dedication as a researcher.

Dr. Bettina Mittendorfer to Lead the Longevity Research Program

The Longevity Research Program, the Longer Life Foundation-funded program at Washington University that focuses on the impact of nutrition and metabolism on longevity, aging, and cognition, has appointed as director Dr. Bettina Mittendorfer. She is also a past recipient of funding from the **Longer Life Foundation** with research interests, among other topics, in metabolic regulation and obesity.

Research Grants Update

LLF's most recent Call for Applications resulted in a near record-breaking 29 new Letters of Intent, in a broad range of areas, in addition to three requests for a second year of funding from current grantees. Individuals receiving funding for 2019-2020 grants will be announced in the next issue of *ReFlections*.

ReCite

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

Treating Disease at the RNA Level with Oligonucleotides
Levin AA. N Engl J Med. 2019 Jan 3; 380(1): 57-70.
https://www.nejm.org/doi/10.1056/NEJMra1705346

This "frontiers in medicine" review article describes recent advances in therapeutics being realized, both potentially and in actuality, through the use of oligonucleotides directed at the RNA level. Therapeutic nucleotides are usually 15-30 nucleotides in length and are designed to be complementary to a specific region of messenger RNA (mRNA). They can cause destruction of the mRNA, induce changes in pre-mRNA splicing patterns, or change the function of a regulatory RNA. Despite remarkable advances, challenges remain including drug safety and delivery.

Editor's Note: *The development of oligonucleotide therapies has the potential to benefit both patients and insured lives. Novel interventions are now available for diagnoses such as Duchenne's muscular dystrophy and spinal muscle atrophy, which could favorably impact mortality and morbidity outcomes. These types of precision medicine treatments will continue to transform clinical medicine in the coming years.*

Immunotherapy 2.0: Improving the Response to Checkpoint Inhibitors
Friedrich MJ. JAMA. 2019; 321(2): 131-3.
https://jamanetwork.com/journals/jama/article-abstract/2719519

This perspective article reviews the history of cancer immunotherapy and discusses the limitations and new directions of these novel treatments. The author also discusses the possible influence of the gut microbiome, combination therapy, and earlier use strategies.

Editor's Note: *The recent developments in cancer screening, diagnosis, and treatment will undoubtedly impact cancer's incidence, morbidity, and mortality rates. Insurers need to keep up with these innovations and model their impact on pricing assumptions and outcomes expectations.*

Global, Regional, and National Burden of Suicide Mortality 1990 to 2016: Systematic Analysis for the Global Burden of Disease Study 2016
Naghavi M. BMJ. 2019; 364:194.
https://www.bmj.com/content/364/bmj.l94

According to this systematic analysis, suicide continues to be an important cause of preventable mortality worldwide. Annual deaths from suicide increased by 6.7% over the 27-year period, but global age-standardized suicide mortality decreased by 32.7%; however, there is considerable regional variation. In addition, recent trends in the U.S. indicate worsening rates over this time period.

Editor's Note: *Suicide is a tragic and preventable cause of death. Insurers should seek ways to help reduce and eliminate this epidemic. While macro trends appear favorable, local and regional data should be assessed in order to establish optimal underwriting and pricing approaches.*

Integrating Genomics into Healthcare: A Global Responsibility
Stark Z, et al. American Journal of Human Genomics. 2019 Jan 3; 104(1), 13-20.
https://www.ncbi.nlm.nih.gov/pubmed/30609404

According to this commentary, written by an international group of authors, genomic data from more than 60 million patients is expected to be generated within healthcare over the next five years. They also note that since 2013, 14 governments have spent US$4 billion on genomic-medicine initiatives and on transitioning genomic testing into mainstream medical practice. The paper details the diversity of efforts in various countries around the world to accomplish this task and provides a framework for international cooperation to accelerate implementation.

Editor's Note: *The rapid growth and development of genomic medicine initiatives worldwide will impact insurers everywhere. It is hoped that this new era of medicine will improve both quantity and quality of life. There is much work to be done, but the benefits to both society and insurers will likely be realized in the not-too-distant future.*

Measles, Mumps, Rubella Vaccination and Autism: A Nationwide Cohort Study
Hviid A et al. Annals of Internal Medicine. 2019 Mar 5.
https://annals.org/aim/fullarticle/2727726/measles-mumps-rubella-vaccination-autism-nationwide-cohort-study

This study used Danish population registries to link information on MMR vaccination and autism diagnoses along with other vaccines and sibling history of autism. Hazard ratios were estimated. Results showed MMR-vaccinated children compared with MMR-unvaccinated children demonstrated a fully adjusted autism hazard ratio of 0.93 (95% CI, 0.85-1.02). The study strongly supported the hypothesis that MMR vaccination neither increases the risk of autism nor triggers it in susceptible children.

Editor's Note: *Given the prevalence of anti-vaccine campaigns it is important to review the data and science, which generally refutes the risks promoted by those opposed to vaccine use. While the impact of the anti-vaccine movement has likely been minimal to insurers to date, surveillance should continue, especially as the popularity of living benefits for children products continues to grow.*

MEDICAL TEAM UPDATE

Dr. Kar-Neen Tam, MBBCh PgDp MSc, has joined RGA as a medical consultant for the Asia Pacific region. Her medical underwriting experience includes her most recent position as Chief Medical Officer for Professional Provident Society (PPS) South Africa. A graduate of the University of the Witwatersrand in South Africa, she has extensive clinical experience in general medical and specialist diabetes care. She is also interested in non-communicable disease management and in nutrition and lifestyle modification as preventive therapies.

Dr. John Lefebre, Vice President, Medical Director, has recently transitioned from full-time consultant to full-time RGA associate. He is a member of RGA's Global Support Team.

PROMOTIONS

Dr. Sheetal Salgaonkar and **Dr. Georgiana Pascutiu** have been promoted to Vice President and Medical Director, Global Support Team. Dr. Salgaonkar is based in Mumbai, India, and Dr. Pascutiu is based in Toronto, Canada.

RGA THOUGHT LEADERSHIP PUBLICATIONS

RGA publishes content on many topics relevant to medical underwriters. Here are links to some recent publications:

1. Global Health Brief: Fetal Monitoring, by Dr. Elizabeth Gil
   https://www.rgare.com/knowledge-center/media/articles/global-health-brief-fetal-testing
2. White Paper: Genetics and Insurance: Challenges and Opportunities II, by Dr. John Lefebre, Dr. Georgiana Pascutiu, Dr. Sheetal Salgaonkar, and Dr. Daniel D. Zimmerman
   https://www.rgare.com/knowledge-center/media/research/genetics-and-insurance-challenges-and-opportunities-ii
3. White Paper: Lifestyle-Related Behaviors and Mortality: A Comparison of Physical Inactivity and Smoking, by Julianne Callaway, Jason McKinley, Richard Russell, Guizhou Hu, and Kishan Bakrania
   https://www.rgare.com/knowledge-center/media/research/lifestyle-related-behaviors-and-mortality-a-comparison-of-physical-inactivity-and-smoking
4. Precision Medicine and Targeted Cancer Therapy, by Dr. Lisa Duckett
   https://www.rgare.com/knowledge-center/media/articles/precision-medicine-and-targeted-cancer-therapy

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The security of experience. The power of innovation.