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This edition highlights groundbreaking research on how the brain is controlling the aging process, how population-wide salt reduction could have a significant effect on mortality, how alcohol intake in England is increasing liver disease deaths and an update on the new Middle East respiratory syndrome coronavirus (MERS-CoV).



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RMS will shortly be releasing its 2013 updated Longevity Risk Model.

The RMS Longevity Risk Model is being updated with the latest published mortality data. The quantity of scientific and medical research into the causes of mortality improvement that RMS is using has now increased significantly and is also being used to re-parameterize the model.

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ONE STEP CLOSER TO SIGNIFICANT LIFE EXTENSION

New research has demonstrated that the brain controls the process of aging in mice. By tweaking mechanisms in the brain's hypothalamus, scientists were able to extend the lives of mice by 20% without the animals suffering from muscle weakness, bone loss, or memory problems common in old age.

If this research is replicated in humans and drugs are discovered to extend human lifespan, this would add an extra 15 years of life to the current U.S. average life expectancy of 78.7 years.

This new scientific discovery, published in the journal *Nature* in May 2013, shows that the process of aging might not just be a degenerative process, but may be controlled by the brain. Scientists discovered techniques to manipulate age-related signaling pathways to both increase and decrease levels of a protein called NF-kB. The lifespan of the mice was extended without the animals suffering from muscle weakness, bone loss, or memory problems, which are common in old age. By increasing NF-kB levels in mice, researchers were able to speed up systemic aging. In contrast, the opposite was seen by decreasing NF-kB levels. Using physiological, cognitive and behavioral tests, scientists demonstrated that by blocking NF-kB, the lifespan in mice increased by 20%.

This protein complex NF-kB has been shown in the past to influence longevity in flies, as well as reverse skin and blood vessel aging in mice. Research shows that NF-kB is central to many biochemical processes involved with inflammatory processes, which are in turn associated with health problems, such as cardiovascular disease. As a result, the scientists based in Albert Einstein College of Medicine of Yeshiva University, New York focused their research on hypothalamic inflammation.

They discovered that NF-kB is more active in the hypothalamus of mice as they get older. When they blocked the NF-kB pathway in mice, the mice lived up to 1,100 days, compared to 600-1000 for normal healthy mice. When researchers activated the NF-kB pathway, the mice died within 900 days.

Up until now, medical research has shown that the hypothalamus is an area of the brain responsible for growth and metabolism. Scientists have speculated whether aging occurs independently in the body's various tissues or if aging can be controlled by one of the body's organs.

As the body ages, the immune system turns on itself by creating a malfunctioning state of worsening inflammation in the body. Inflammation is evident in various age-related conditions, such as metabolic syndrome, cardiovascular disease, neurological disease, and cancer.

A second discovery was made by scientists when investigating the effects of different levels of NF-kB in the hypothalamus. Increased levels of NF-kB caused decreased levels of another hormone called gonadotropin-releasing hormone (GnRH) in the hypothalamus. This hormone, normally associated with reproduction, was then injected into mice. Increased levels of GnRH protected the mice against impaired neurogenesis, the creation of brain neurons or cells, which is impaired as the body ages. Hormone injections of GnRH in mice were shown to protect against the decline of neurons.

Preventing the hypothalamus from causing inflammation and increasing neurogenesis are two new strategies for scientists to pursue to increase lifespan and treat age-related diseases, such as type 2 diabetes, cardiovascular disease, cancer, and Alzheimer's disease.

Implications for the Life and Pension Risk Industry

Current mortality improvements are being driven largely by erosion of premature mortality from cardiovascular disease. Future mortality improvements will depend on improvements in regenerative medicine and anti-aging research. This recent discovery in anti-aging research that the brain controls the aging process is not only of great interest to scientists but also to people who model longevity in the life and pension industry. If this research is replicated in humans, this could have significant implications for the life expectancy of future pensioners. RMS includes potential future anti-aging treatments in mortality improvement scenarios of its forward-looking GASP longevity risk model. Surveillance of this type of research is an integral part of RMS's medical modeling agenda.

REDUCING SALT INTAKE COULD SAVE THOUSANDS OF LIVES

The United States Centers for Disease Control and Prevention (CDC) commissioned a study to quantify the health benefits of reducing dietary sodium in the U.S. It wasn't a surprise to see that sodium reduction would save lives by reducing heart attacks and stroke rates but it was a surprise to see the amount of lives it saved – approximately a further 2.7% reduction in heart disease-related deaths per year for the next ten years.

Excess dietary sodium can cause high blood pressure or exacerbate it, which leads to CVD, the number one cause of death in the U.S. Sodium intake in the U.S. is estimated to be around 3,500 mg/day. The American Heart Association (AHA) currently recommends a sodium intake 1,500 mg/d for the entire U.S. population. The Dietary Guidelines for Americans suggests a limit of 1,500 mg/d in African-Americans, people 51 years of age and over, and people with hypertension, diabetes or chronic kidney disease, and no more than 2,300 mg/d in all others.

Researchers at three different universities used three different models to estimate how lowering sodium would save lives over a ten-year period examining evidence from direct effects on cardiovascular disease (CVD) mortality, indirect effects mediated by blood pressure changes and lastly by analyzing epidemiological studies.

Three different modeling approaches were used to model the same scenarios:

- Scenario A, gradual uniform reduction totaling 40% over 10 years
- Scenario B, instantaneous 40% reduction in sodium consumption sustained for 10 years to achieve a population-wide mean of 2,200 mg/day
- Scenario C, instantaneous reduction to 1,500 mg sodium per day sustained for 10 years

Results from scenario A estimated across the three models that between 280,000 to 500,000 deaths could be saved over the next ten years. In the B and C scenarios where there was an instantaneous reduction in sodium initially, between 0.7 and 1.2 million deaths were estimated to be avoidable in 10 years if sodium consumption fell to recommended guidelines.

In the most extreme scenario, researchers estimated that CVD deaths for U.S. males and females age 35-45 would be 5.1 million. In this scenario it was also estimated that there would be 16.7 million all cause deaths for U.S. males and females aged 35-45. Researchers estimated that 24 % (1.2 million) of CVD related deaths over the 10 years were avoidable.

Sodium is a component of salt. A half a teaspoon of salt contains 1,000 milligrams of sodium. A small amount of sodium is naturally present in most foods, but most dietary sodium is found in processed foods in the form of salt. It is an inexpensive way to boost the flavor of processed foods and in some cases acts as a preservative.

The study does not address how sodium reduction would be achieved – whether through voluntary reductions or through possible federal regulations. In 2010, the Institute of Medicine recommended that the Food and Drug Administration (FDA) regulate sodium in food. However, under the current federal U.S. law, salt is an unregulated food ingredient because it is generally regarded as safe by the FDA. U.S. policymakers are working more with the food industry to decrease sodium content in food items. Through the National Salt Reduction Initiative (NSRI), a partnership of more than 90 city and state health authorities and 21 companies have elected to reduce sodium in popular food products by 2014. Kraft recently announced a three-year commitment to reduce sodium across its products by 10 percent and Heinz reduced sodium

across its Ketchup base product line by 15 percent.

Over the past few months experts have disagreed over salt reduction targets for all. The Journal of the American Medical Association reported that healthy men and women who ate more sodium than average weren't at higher risk of dying of heart disease or stroke. Some experts believe that the balance of sodium and potassium impacts mortality more. Clearly more research is needed. In the meantime the targets for sodium and salt reductions have not changed.

Implications for the Life and Pension Risk Industry

Studies show that excessive salt consumption accounts for thousands of deaths from heart attacks and strokes. A lot of experts believe new regulations to reduce salt in the U.S. are the only way that food companies will reduce sodium faster. National public health programs and regulations to reduce dietary sodium intake could potentially save thousands of lives. RMS tracks how mortality changes as a result of external factors that influence mortality, including organizational and political factors that influence healthcare provision.

LIVER DISEASE DEATHS ON THE RISE IN ENGLAND

Deaths from liver disease and liver cirrhosis in England have risen 25% between 2000-2009, while falling elsewhere in Europe. This is in contrast to other major causes of death, which have been declining. Although numbers of deaths due to heart disease and cancer are much greater, liver disease kills people at a much younger age. According to the authors of a report by the National End of Life Care Intelligence Network in the U.K., heavy drinking, obesity and hepatitis C and B are the main causes.

In England, 2% of deaths between 2001 and 2009 were from liver disease. Most liver disease deaths are preventable. Upon closer inspection, most deaths from liver disease were in people under 70 and more than one in ten of deaths of people in their 40s are from liver disease. More men than women die from liver disease - 60% are men and 40% are women. Alcoholic liver disease accounts for well over a third (37%) of liver disease deaths.

In the U.K. the current annual death rate from alcohol-related conditions is more than three times that for deaths in road accidents. Alcohol is considered one of the three biggest lifestyle risk factors for disease and death in the U.K after smoking and obesity. Recent reports suggest it has become acceptable to use alcohol for stress relief, especially in middle aged professionals, putting many people at risk of chronic diseases.

Age breakdown results in the report show that the average annual number of alcoholic liver disease deaths is greatest in the 50-59 age group. The Office for National Statistics (ONS) reports that age-specific alcohol-related death rates were highest for those aged 55 to 59 and lowest for those less than 30.

Middle-aged drinking patterns may be a cause for increased deaths according to recently published studies. According to the ONS, more than 13 per cent of adults over 45 drink every day compared with just four percent of those under 45. As people get older they tend to drink more often - with over 22% of men aged 65 and over drinking almost every day compared with just three per cent of men aged 16 to 24. Among women, 12 per cent of over-65s drink alcohol almost every day compared with just one percent of young women aged 16 to 24.

There are three times as many deaths from alcoholic liver disease in the most deprived areas when compared to the least deprived areas. The highest number of liver disease deaths is in the North West (1,899), South East (1,503) and London (1,424).

Back in the early 1990s, alcoholic drinks called Alcopops, which were marketed towards the young, caused a wave of public concern that led to the government introducing regulations and a 40% tax on Alcopops. This resulted in their demise. Still however, the levels of binge drinking among 15-16 year olds in the U.K. compares poorly with many other European countries. Binge drinking in adolescence was associated with increased risk of health, social, educational and economic adversity continuing into later adult life. Recent reports showing deaths from alcohol-related disease in young women are rising; contrary to the overall trend and is a worrying statistic for the U.K.

Recommendations set by U.K. Chief Medical Officers suggest no more than four units per day for men and three units a day for women. The Royal College of Physicians recommends weekly alcohol limits of 21 units for men and 14 units for women.

Implications for the Life and Pension Risk Industry

The World Health Organization lists alcohol as the third leading risk factor for premature death in developed countries, with only tobacco and blood pressure causing more premature death and disability. If deaths from liver disease continue to grow, this may have significant implications for mortality projections in the U.K. RMS will be tracking closely the U.K. government's response to these recent increases in premature deaths.

MERS-COV - LETHAL VIRUS WITH UNKNOWN SOURCE OF INFECTION

Cases of the novel coronavirus, now known as the Middle East respiratory syndrome coronavirus (MERS-CoV), are continuing to steadily increase. To date, the World Health Organization (WHO) has reported nearly 132 laboratory-confirmed cases, with approximately 50% of these fatal.

Any virus with such a high case fatality rate causes alarm among public health officials.

Most of the cases have been detected in Middle Eastern countries, with a majority in Saudi Arabia. However, there have also been a few cases in Europe (France, Germany, Italy, and the U.K.), in people that traveled to Middle Eastern countries. People of all ages have fallen ill due to the MERS-CoV, with a median age of cases at 51 years, but the majority of cases have been in elderly men. Infection with the virus has also been more common in those with underlying health conditions.

Coronaviruses are common respiratory pathogens, and many cases of the common cold are caused by these types of viruses. However, the novel MERS-CoV (which belongs to same viral family) causes a more severe acute respiratory infection, with symptoms similar to SARS, including pneumonia and sometimes kidney failure. Currently, no approved antiviral therapy or vaccine is available, and treatment is limited to supportive care.

The source of infection for MERS-CoV is unclear. Investigators are trying to identify its source to limit the spread. One study has shown that camels may be a possible animal reservoir. Bats are also suspected as a source of infection. Limited human-to-human transmission has been seen, primarily in situations where family members are taking care of a sick individual or in hospital settings where healthcare workers have gotten infected from being exposed to sick patients.

More cases are now being detected as part of the routine surveillance that is being done around contacts of known severe cases. With the latest cases reported, what is known about the epidemiology of the virus is changing—the demographics of the current cases skew younger and more female cases are now being seen, and less severe symptoms and milder cases are now being seen. Although milder cases is good news, the possibility of asymptomatic cases (those infected but not experiencing symptoms) transmitting the virus unknowingly could lead to higher transmission rates.

These trends are similar to those seen when the SARS coronavirus first emerged in 2002-2003. Initially a higher case fatality rate was observed, and higher fatality rates were occurring in the elderly. But unlike SARS, fewer healthcare workers are getting sick from the MERS-CoV, possibly because of better infection control measures being implemented since the SARS outbreak. Public health officials are concerned of the possibility of “superspreaders” of MERS-CoV, like that seen during the SARS outbreak. There is also concern over whether there are adequate surveillance and preparation measures in place in regions where the virus is transmitting.

Health officials are warning pilgrims making the journey to Mecca, Saudi Arabia for the upcoming annual Hajj in October to take precautions to decrease risk of spreading infectious diseases such as the MERS-CoV. Mass gatherings are often associated with increased health risks. Usually between 2-5 million people attend this event. To keep the numbers down, Saudi authorities have reduced entry visas by a fifth. The WHO is not currently recommending any travel or trade restrictions at this time.

The WHO has recently convened a new emergency committee of international health experts to monitor the MERS-CoV situation and make recommendations to respond to the evolving risk. At the same time, the committee is also closely monitoring the novel H7N9 flu situation, as well as continuing to monitor the H5N1 avian flu situation. Although these three viruses are unrelated, they are all highly pathogenic, have the ability to mutate to become more transmissible, and therefore all have pandemic potential.

Implications for the Life and Pension Risk Industry

RMS information is provided to insurance risk professionals to assist them with their risk management, loss reserving and capital management decisions. In the case of MERS-CoV, without sustained human-to-human transmission, RMS will not change probability assumptions for its RMS® Infectious Disease Model. RMS will monitor the evolving situation closely and will post updates as more information becomes available.

OTHER NEWS IN BRIEF

World Health Organization Proposes New Pandemic Flu Alert Levels

In June 2013 the World Health Organization (WHO) proposed a new pandemic alert system which will focus more on disease risk as opposed to geographic spread. The current six-phase system currently used by the WHO will be replaced by a four-phase alert system.

- **Interpandemic:** The period between pandemics
- **Alert:** When a new pathogen subtype has been identified and increased vigilance and risk assessment are warranted
- **Pandemic:** A period of global spread of a new subtype as indicated by global risk assessment based on virologic, epidemiologic, and clinical data.
- **Transition:** Global risk drops, prompting global actions and response activities

The new pandemic levels incorporate lessons learned from the 2009 H1N1 pandemic, when the previous alert system relied on disease spread. The declaration of a pandemic will now be based on risk and severity assessment.

Serendipitous Marine Discovery of New Antibiotic

Serendipity has come to the aid of microbiologists struggling to find new classes of antibiotics. Professor William Fenical, with colleagues from the University of California San Diego's Scripps Institution of Oceanography, discovered a new antibiotic compound in sediments close to shore off the coast of Santa Barbara, California. Anthracimycin is a marine microbe-derived antibiotic that has the ability to kill the anthrax bacterium and other deadly pathogens. Particularly exciting is that Anthracimycin has a new and unique chemical structure, which also helps to explain why its discovery in a pharmaceutical laboratory would have been so very unlikely.

Eating Light to Live Long - Oldest Man Dies at 116

A Japanese man recognized as the world's oldest living person died of natural causes in June 2013. Mr. Kimura was born on 19th April 1897, the same year as aviator Amelia Earhart.

He had 7 children, 14 grandchildren, 25 great-grandchildren, and 13 great-great-grandchildren. After retiring from the local post office he worked with his son on his farm until he was 90.

When interviewed by Journalists in Japan, Mr. Kimura attributed his longevity to "eating light to live long". His granddaughter-in-law also attributed his longevity to his positive mental outlook on life.

Potential New Treatment for Pancreatic Cancer

Researchers from the Albert Einstein College of Medicine in New York City used genetically modified bacteria to deliver radiation to cancerous pancreatic tissue in mice. Results showed dramatic improvements as pancreatic tumors shrunk and metastatic cells was reduced by 90% halting the spread on the disease.

Despite the advances made against many types of cancer, pancreatic cancer still has one of the worst prognoses. Survival rates are pretty grim with only around 4% of patients surviving for 5 years. In the U.S. the number of new cases of pancreatic cancer every year is around 40,000, and the number of deaths every year is 40,000.

For reasons, many of them still unknown to scientists, pancreatic cancer spreads easy to other parts of the body. Any new research that helps scientists better understand pancreatic cancer spread brings us closer to a cure.

Bowel Cancer up 30% For Men in 35 Years

According to Cancer Research U.K., bowel cancer rates have increased by nearly a third in men, and by 6% in women, over the past 35 years in the U.K. Increasing rates of bowel cancer are linked to our lifestyles, obesity and the consumption of diets high in red and processed meat and low in fiber. Experts are somewhat puzzled by the increase in numbers and in particular the differences between men and women.

New Embryonic Stem Cells Techniques Restore Sight in Blind Mice

For the first time photoreceptors were grown from embryonic stem cells and were successfully transplanted into the retinas of mice giving people who are blind due to photoreceptor damage hope to restore their vision in the future. Sourcing donor photoreceptor cells is difficult and so scientists instead decided to make their own. Photoreceptor damage causes diseases such as age-related macular degeneration, retinitis pigmentosa and diabetes-related blindness.

The transplanted cells matured and connected with nerves, which transmitted visual signals to the brain. These scientists are already working on how to repeat this procedure with human stem cells and have already grown the precursors to the human retinal photoreceptor cells.

The scientific process of trying to connect photoreceptors with the damaged retina has been going on for the last ten years and scientists at University College London's Institute of Ophthalmology and Moorefield's Eye Hospital estimate that it is going to take another 5 years before this technique is safe to use on humans.

OTHER NEWS IN BRIEF

Dementia Rates Fell From 8.3% to 6.2% Over 20 years

Despite all the predictions that Alzheimer's disease is about to explode, researchers from Cambridge University have just announced results of a study indicating that there is a lower prevalence of dementia today when compared with dementia prevalence in the 1990s.

Dementia rates were analyzed in 7,600 people in the early 1990s and compared to rates in a contemporary group of similar characteristics. The results were consistent across age groups and gender.

In the 1990 study, 8.3 % of people met all the criteria for dementia. In the new findings, that fell to just 6.2 percent.

The reason for the decreasing rates is very likely due to a healthier and better-educated population and longer lifespans. Data shows that the rates of dementia are linked to education rates and heart disease management. People who control their blood pressure and cholesterol levels are less likely to get dementia.

RISK MANAGEMENT SOLUTIONS FOR THE LIFE & HEALTH INSURANCE INDUSTRY

Risk Management Solutions (RMS) applies the latest science in analytical tools for making risk management decisions in the life and health insurance industry, including management of excess mortality and longevity risk.

RMS provides RMS LifeRisks™, a modeling platform for the life insurance and pension risk management industry. RMS LifeRisks enables companies to assess an integrated view of trend and shock risks into their life and annuity portfolios that is underpinned by detailed medical research and social change projections RMS Models.

RMS models include probabilistic stochastic simulation of mortality shocks arising from influenza pandemic, emerging infectious diseases, terrorism mass mortality and group life concentration risk analysis, natural catastrophes and other sources of mass mortality. RMS also provides a longevity risk model comprising probabilistic stochastic models of mortality improvement scenarios. RMS models are designed to provide holistic assessments of mortality risk to enable diversification benefits, risk capital hedging between mortality and longevity risks, and other analyses to be quantified.

RMS produces excess mortality coverage for most countries with significant life insurance markets. RMS Longevity Risk models are available for United States, United Kingdom, Canada, Netherlands, France and Germany.

Consultancy Services

RMS provides consulting services to help clients across many areas of risk management. Projects include economic capital requirements, Solvency II internal model calibration and approval, insurance product

design, risk transfer and de-risking strategies, and reinsurance optimization. RMS acts as Modeling Agent on capital market transactions. RMS has just conducted the risk analysis for a catastrophe bond recently issued through Atlas IX Capital Ltd. The bond, Atlas IX Capital Limited (Series 2013-1), sponsored by SCOR, transfers \$180 million of U.S. excess mortality risk to the capital markets.

<http://www.rms.com/about/newsroom/press-releases/>



RMS New Showcase Feature

New Approach to Hedging Analytics released in RMS LifeRisks platform. Scenario approach to quantifying Mortality/Longevity hedge now gives insurers improved risk capital efficiency.

Publications (login required for RMS Liferisk's library)

Annuities: of wealth and health: by Gordon Woo published in The Actuary Magazine, April 2013

<http://www.theactuary.com/features/2013/04/of-wealth-and-health/>

Antibiotic Resistance: Evolving Threat: <http://www.rms.com/resources/publications/liferisks> Go to Alerts

Longevity Risk: The Impact of Daily Aspirin Intake on Pension Liabilities: <http://www.rms.com/resources/publications/liferisks> Go to Papers

For more information and publications visit www.rms.com/liferisks

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ABOUT RMS

RMS is the world's leading provider of products, services, and expertise for the quantification and management of catastrophe risk. More than 400 leading insurers, reinsurers, trading companies, and other financial institutions rely on RMS models to quantify, manage, and transfer risk. As an established provider of risk modeling to companies across all market segments, RMS provides solutions that can be trusted as reliable benchmarks for strategic pricing, risk management, and risk transfer decisions.