depends partly on the degree of genetic difference between an organ and its recipient. The human leukocyte antigen (HLA) system genes (or gene complex), which governs compatibility, are located on the short arm of the chromosome 6, and encode the major histocompatibility complex (MHC) proteins. These proteins are divided into class I (HLA A, B and C) and class II (HLA DR, DQ and DP) antigens and are responsible for regulating the human immune system. The role of these proteins is to present peptides to T-cells, enabling them to recognize and eliminate “foreign” cells. The most common form of acute rejection of grafts involve a recipient’s T-cells (i.e. adaptive immune response)

immunosuppressive drugs. Later graft loss is usually due to a combination of factors, including pre-existing donor disease, recurrence of the recipient's kidney disease, and the recipient's immunologic response to the new organ. Chronic rejection, another major long-term cause of graft loss, is characterized by slow, progressive renal function deterioration that cannot be altered by common antirejection drugs.

Recurrent Disease

Recurrent renal disease affects as many as 10% of kidney transplant recipients. It accounts for fewer than 3% of all graft losses,[5] and is also the third most frequent cause of graft loss at 10 years after transplantation in patients with underlying GN. Although IgAN, the most common type of GN, histologically recurs in up to 60% of kidney transplant patients, only about 5% will lose their graft as a result of its recurrence. Recurrent focal segmental GN and membranoproliferative glomerulonephritis, however, are associated with high risk of graft loss.

ESKD patients with Alport Syndrome receiving renal replacement therapy (RRT) usually have excellent graft survival rates. They also have superior patient survival rates while undergoing dialysis and superior patient and graft survival after transplantation from a deceased donor compared with patients receiving RRT because of other causes of kidney failure. This superior survival might be explained by the lack of additional organ system involvement in Alport Syndrome and the non-recurrent nature of the disease.[10] Although individuals with Alport Syndrome are thought to benefit from the non-recurrent character of their disease in their kidney grafts, about 2% to 5% of them will develop anti-glomerular basement membrane (GBM) disease early in the post-transplant period, resulting in rapid graft loss.

Diabetic nephropathy can also recur in renal grafts. Time to onset is similar to that seen in native kidneys. This condition is generally an uncommon cause of graft loss.

Patient and Graft Survival by Source of Graftm4.m4.

The quality of the graft has a direct effect on important clinical outcomes such as acute rejection, delayed graft function, and patient and graft survival. Recipients from related living donors have a lower mortality than recipients from deceased donors, likely because of lower rates of rejection episodes thus less complex immunosuppressive drug regimens.

According to the Scientifc Registry of Transplant Recipients, in 2015, the fve-year survival for patients who received a deceased-donor kidney in 2010 was 86.8% and for living-donor recipients was 93.5%. Survival was lower in recipients age 65 years and older and in recipients with diabetes as cause of kidney failure.[5] Fifteen-year graft failure among adult living donor transplant recipients was 37.3% (1990-2005) and 52.8% for adult deceased donor transplant recipients.[11]

Expanded-criteria donor (ECD) kidney longevity is believed to be much shorter, with the kidney's half-life estimated at six to eight years, compared with 10 to 12 years for a non-ECD kidney from a deceased donor.[12] ECDs are less-than ideal donors – over age 60 or age 50 to 59 and have two of the following: hypertension; terminal serum creatinine >1.5

References

1.

SEASONAL INFLUENZA AND MORTALITY

Abstract

This article follows up on two older articles by RGA associates: "Seasonality of Mortality," by Kyle Nobbe, published in the January 2017 edition of ReFlections,[1] *and "Seasonal Flu and the Impact on Mortality," by Dr. Dave Rengachary.*[16]

samples were positive for it. Each column indicates 5th, 25th, 75th and 95th percentiles, as well as median and average. H3 dominance was assessed in June and September, when only global data were available, and in November and January, when U.S.-specifc information was also available.

At each observation point, for influenza seasons during which an H3 strain dominated, the mortality experience was significantly worse than otherwise. If an H3 strain was dominant globally in June, a 52% increase in excess mortality due to influenza would have been expected in the upcoming influenza season. If it was still dominant globally in September, it would have been associated with a 66% increase. In the U.S., as indicated above, data are only available after October. If an H3 strain was dominant in November, it would be associated with a 130% increase in excess mortality due to influenza. This effect was not observable in our model for January, possibly because much of the season's influenza mortality would generally have already occurred by then.

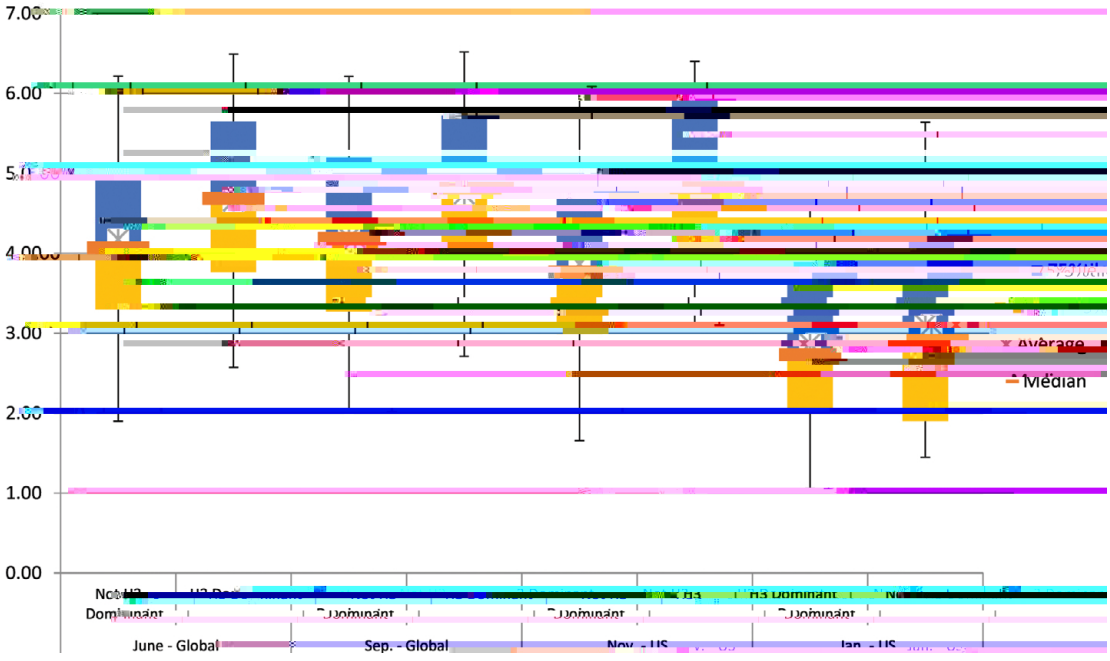
Vaccine Match

Vaccines work by generating an immune response in the human body to the strains and subtypes incorporated into the vaccine. An influenza vaccine will typically contain three or four strains and subtypes: an H1 subtype, an H3 subtype, and one or two B strains. If the H1 type in the vaccine matches the type that is circulating, but the H3 type does not, the vaccine protects against the circulating H1 but not the H3.

Sometimes the immune response that develops from vaccination results in strong protection against influenza viruses circulating duration an influenza season, and at other times the protection is weaker. The strength of an immune response to a vaccine can be assessed in a laboratory using a test that determines how effectively antibodies generated by the immune system in response to the vaccine inhibit a sample of influenza virus. In our model, a vaccine is considered "matching" if greater than 90% of the isolates (virus samples cultured from sources) were an antigenic or genetic match for the strains and subtypes incorporated in the vaccine.

Because this is a laboratory test, the antigenic match may not alway52uoy53lod pre(human body to m

Figure 3: Log Excess Mortality Rate by H3 Dominance and Models



Source: BlueDot, RGA

Influenza vaccine effectiveness cannot be measured until influenza is circulating in the northern hemisphere, so early and interim measures of effectiveness against test-positive influenza are generally not available until January or February, and final estimates are not available until well after influenza season is over.

This may change in the future. Rec€U p‰SD„Ae7W&R‰cu&Ve—"˜3pm¢hµF±t'6®¶e

seasonality will be seen). Thanks to different monitoring programs around influenza activities, indicators can be used for early warning or ongoing monitoring purposes. Although it is not currently possible to predict excess influenza-attributable mortality with accuracy, a high-level assessment of the general mortality experience may be possible prior to or early in an influenza season by examining early warning signs of severe influenza mortality.

Although the correlations between different indicators and influenza mortality may help predict influenza season severity, it is important to gain a better understanding of the underlying reasons for these relationships. Otherwise, we risk missing changing population trends. For example, as discussed above, people have been shown to develop a more robust immune response to the first influenza strains they encounter in their lifetimes. The current older generation, who are most vulnerable to seasonal influenza-associated mortality, encountered H1-dominated influenza seasons in their childhoods, making them more vulnerable to H3 infections. As populations age, and the older population transitions to individuals whose first exposure was to influenza of a different subtype (e.g., H3N2), this correlational relationship might also be expected to change. Additionally, there are other factors that may contribute to influenza severity but cannot currently be used as early-warning indicators. For instance, weather is believed to play a role in influenza season onset,[15] and so may potentially influence the impact of other indicators on the seasonal pattern of mortality.

Most studies of population-level indicators of risk have focused on the general population. The U.S. influenza mortality data used in our model are only available for the general population, which may have differences in age distribution, health status, and access to healthcare compared to the insured population. Because of this, population level indicators of risk may affect an insured population differently from the general population. Hence, it is also important to understand individual-level risk factors. Although they are unlikely to cause marked effects in season-to-season influenza mortality, they may explain differences between the general and insured populations.

1. Kyle Nobbe, Seasonality of Mortality, RGA Reflections, January 2017. http://www.rgare.com/docs/default-source/newsletters-articles/reflections-vol-40-jan-2017.pdf?sfvrsn-0
2. National Center for Immunization and Respiratory Diseases. 2015. Chapter 12: Influenza. In: Epidemiology and Prevention of Vaccine-Preventable Diseases. Accessed online on November 11, 2016 at http://www.cdc.gov/vaccines/pubs/pinkbook/flu.html
3. Matias G, Taylor R, Haguinet F et al. Estimates of mortality attributable to influenza and RSV in the United States during 1997-2009 by influenza type or subtype, age, cause of death, and risk status. Influenza Other Respir Viruses. 2014 Sep, 8(5), 507–15. https://www.ncbi.nlm.nih.gov/pubmed/24975705
4. Belongia EA et al. Effectiveness of inactivated influenza vaccines varied substantially with antigenic match from the 2004-2005 season to the 2006-2007 season. J Infect Dis. 2009 Jan 15;199(2): 159-67. https://www.ncbi.nlm.nih.gov/pubmed/19086915
5. Ndifon W, Dushoff J, Levin SA. On the use of hemagglutination-inhibition for influenza surveillance: surveillance data are predictive of influenza vaccine effectiveness. Vaccine. 2009 Apr 21; 27(18): 2447-52. https://www.ncbi.nlm.nih.gov/pubmed/19368786
6. Tricco AC, Chit A, Soobiah C, et al. Comparing influenza vaccine efficacy against mismatched and

Sepsis	Suspected or documented infection + an acute increase of >2 SOFA* points
Septic shock	Sepsis and vasopressor requirement to maintain mean arterial pressure (MAP) >65 mm Hg + lactate >2 mmol/L (18 mg/dL) despite adequate fuid resuscitation

*SOFA = Sequential Organ Failure Assessment. This score weighs data on respiratory, coagulation, liver, cardiovascular, central nervous system, and renal

Q: How and why does CR result in increased lifespans?

A: CR results in increased lifespans by lowering the levels of several growth factors and hormones that drive cellular proliferation, which ultimately reduces the risk of damage to the body. For example, if insulin, testosterone, and inflammatory drivers are reduced, the organism benefits through increased genomic stability, and cells are made younger and less dysfunctional. C04800465senescence is also decreas

Q: Life expectancy and maximum life span are different. What do you think is the maximum human lifespan?

A: Everyone has a genetic predisposition for disease/aging, but if a person does everything right, they might be able to live longer than what their genes might determine. Right now, the maximum confirmed life span is 122 – the age at which Jeanne Calment,

ReCite

recently appearing in the literature...

The Cumulative Burden of Surviving Childhood Cancer: An Initial Report from the St. Jude Lifetime Cohort Study (SJLIFE)
Bhakta N, et al. The Lancet. 2017 Dec 9; 390(10112): 2569-82.
http://dx.doi.org/10.1016/S0140-6736(17)31610-0

This study followed 5,522 ten-year survivors of childhood cancer and assessed the cumulative burden of chronic health conditions (CHCs) in comparison with community controls. The results demonstrated that survivors have twice the burden of disease (by an excess of seven more CHCs) at age 45 compared to the general population. The burden, however, is quite variable and depends on the type of cancer, the type of treatment received, age at diagnosis, and treatment era.

Editor's Note: *Given ongoing success in the treatment of childhood cancers, insurers are seeing increasing numbers of adult survivors applying for many types of insurance products. This paper serves*