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The future of life expectancy

Forecasting long-term mortality improvement trends for insurance

Contents

Executive summary

Human longevity is one of the great success stories of the past century, and there is broad consensus that there are further gains to come. Mortality improvement forecasts underpin the insurance industry's long-term mortality and longevity lines of business. To generate long term forecasts, defined as beyond 20 years, a holistic view of the factors that influence mortality is considered a better predictor than historical data alone. This approach combines analyses of past trends with a forward-looking view of medical advances, societal changes and technological developments.

Life expectancy typically improves in waves as innovations in medicine, healthcare and lifestyles sweep through countries at different times and rates. For most of modern history this has been a cyclical process, resulting in periods of high annual increases in mortality improvement followed by periods with very little improvement each year, and creating a consistently positive trajectory for lifespans over the long term.

The last large wave of high improvement in life expectancies, driven largely by improved diagnosis and treatment of cardiovascular diseases (CVD) and cessation of smoking, ended in about 2010. Since then, population mortality improvement has slowed or plateaued in many advanced markets. Identifying the factors that may produce the next major wave of mortality improvement is important for insurers, to support actuarial assumption setting for both pricing and valuation, and risk management.

The largest positive impact is likely to come from advanced cancer diagnostics and the evolution of treatments from generic to personalised, precision medicine. With fewer opportunities left to revolutionise cardiovascular medicine, decreases in CVD deaths are likely to come from improvements in lifestyle and behavioural risk factors.

As societies age, we expect neurodegenerative and ageing diseases to become incrementally a more significant cause of death. Medical solutions for Alzheimer's disease and dementia are likely to be essential to deliver sustained mortality improvement, since most therapies today typically offer only symptomatic relief. Yet while the potential is vast, such solutions are largely uncharted territory at present.

Given the exciting prospect of advancements in medicine and healthcare, we see the potential for global average life expectancy to reach new milestones in the coming decades. However, lifestyle factors, particularly rising rates of obesity and diabetes due to poor diet and sedentary behaviour, could put future gains at risk. Policy interventions will be key. Innovations in weight loss drugs and surgery may also offer some emerging solutions and we anticipate a small positive impact on mortality trends on the current development path.

In recent years, we note a divergence in mortality trends by socioeconomic status, notably in the US. While premature death rates for lower socioeconomic groups have historically been higher, the continued divergence in mortality trends is concerning as it implies a growing gap in health and death rates.

As the recent experience of COVID-19 shows, insurers should continue to monitor emerging risks. Future threats could come from known risks such as climate change, or a disease or development yet unknown. Our current environment is one of elevated uncertainty and connected extremes. While we see many reasons to be bullish about mortality gains in the long term, risk management, and reinsurance as a part of it, can play a key role in helping insurers to navigate volatility.

Introduction

We live in a world of seemingly accelerating societal progress. Today, technology enables us to communicate, travel and work to a degree previously out of reach. Our ingenuity has driven medical developments and better public health policies, leading to longer, healthier lifespans, with premature mortality on the decline. Even COVID-19, a novel, highly transmissible disease, was curbed via medical interventions and vaccinations, resulting in a lower global mortality rate than a disease such as this would likely have had before this era of staggeringly fast technological evolution.

Progress has rarely been linear. Advances typically come in waves: a vaccine to stave off infection for the most vulnerable, a new test to detect cancer earlier when it can be treated more effectively, or even a new drug to cure or delay disease. Major global events and societal developments can also accelerate or decelerate medical innovation (see Figure 1).

As a result, each generation can have different experiences of health and ageing, some specific to that cohort, others that build on and are enhanced by the innovations of the past. For example, the Silent Generation and Baby Boomers, who were born or came of age in the years after World War II, are great examples of the longevity progress made in advanced countries. Obesity was rare, even after rationing ended, and frequent physical activity the norm. Conversely, smoking was commonplace, and many of the vaccines, scans and tests that are routine today had yet to be invented or widely used.

Figure 1
Major global developments and medical advancements over the last century
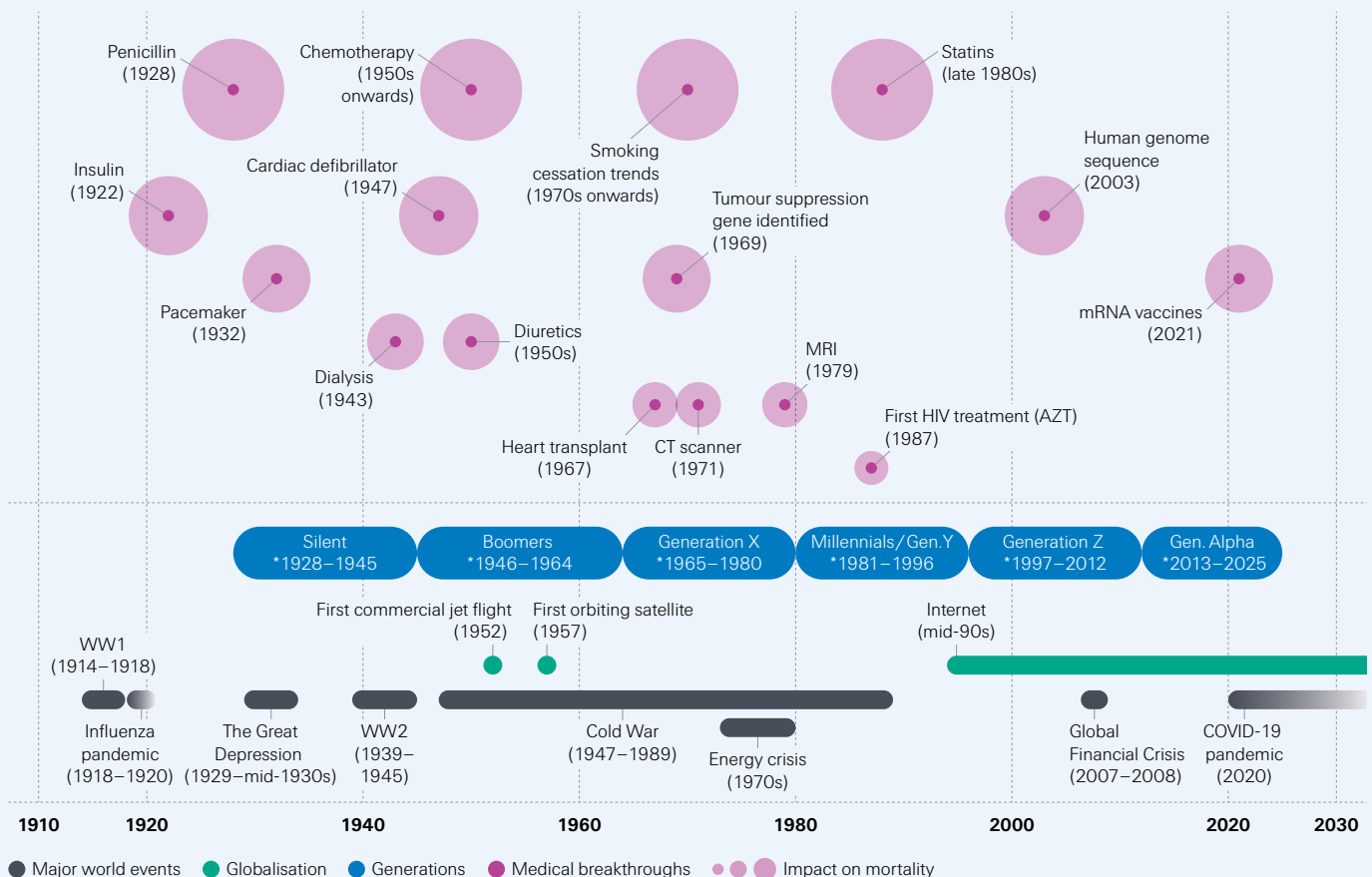

Source: Swiss Re Institute

Today's babies – the new "Generation Alpha" – look forward to a world of unparalleled connectivity, technological advancements, and medical miracles. In many parts of the advanced world, smoking levels have declined over time and access to good healthcare is a given, not a luxury. Yet this generation could also experience poor diets, sedentary lifestyles, high obesity, climate change and increased threats from infectious diseases.

How can mortality improvements be predicted?

For the Life & Health (L&H) insurance industry, tracking such innovations and their impacts over decades is important in the context of building long-range mortality improvement trend assumptions. These assumptions are key, because small deviations in the mortality trend can have significant impacts on an insurer's results over the long term (see Figure 2).

Figure 2

The impact of a range of mortality improvement trend assumptions on a 45 year old UK male's life expectancy

MI set as... — −0.5% — 0% — 0.5% — 1% — 1.5% — 2%
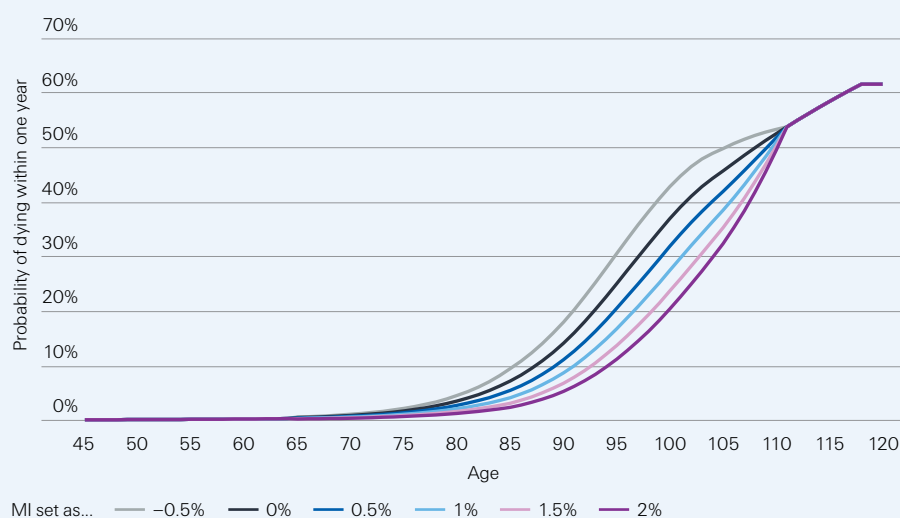
Source: UK S3PMA_L base table. Tapering of mortality improvements uses CMI core assumptions based on a 45-year-old male (linearly to 0% between ages 85–110).

Actuaries and demographers traditionally projected future trend assumptions from past experience data, albeit recognising the uncertainty around this. Today, industry practitioners will typically analyse data from both past outcomes and the expected impacts of emerging trends. By combining expected advances and setbacks, a conclusion can be generated to forecast changes in the trajectory. This approach can be summarised as combining empirical analysis with forward-looking, expert judgement-driven views.

The insured population has historically tended to have better access to healthcare and better baseline health due to underwriting. As a result, it would be fair to assume that medical advancements and global healthcare developments may impact long term mortality improvement trends relatively uniformly across insured segments in every country, even as base mortality rates and short-term mortality trends differ.

This publication examines historical trends alongside future medical advancements and lifestyle factors expected to lead to future mortality improvement, to support insurers' assumption development for advanced markets in the long term.[1]

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[1] Some considerations noted in this paper will also apply to less developed markets, but there are also likely to be significant differences in trajectories, and interpreting results for these markets may require discretion.

Historical mortality improvement: progress in waves

- Lifespans have been in general increasing in most of the world since the early 20th century, with progress in uneven waves.
- The biggest waves of improvements of the past century followed discoveries for treatment of communicable diseases, smoking cessation, and treating and preventing CVD. These significantly reduced premature deaths in all age groups.
- Since 2010, population-level mortality improvement has slowed in several key advanced markets. This primarily reflects a flattening in CVD deaths; the UK is a clear example of this. It is currently unclear what might reverse this, or if CVD mortality improvement may return.
- Socioeconomic factors have a substantial bearing on mortality rates and life expectancy. Higher socioeconomic groups, a proxy for insured populations, have typically benefited from greater mortality improvements than the general population, especially in recent decades.
- In the US in particular, high-income groups have seen higher mortality improvements than the overall population, but these rates of improvement are declining too.
- Countries have seen significant trend reversals in which mortality improvement troughs shift to a strong new wave. Japan made great strides in mortality improvement from the mid-20th century, prior to which it saw little improvement.

Mortality improvement in countries worldwide typically manifests in waves, with periods of high and rapid improvement followed by periods with fewer gains. Since the 1960s, advanced markets have experienced multiple waves in mortality improvement from peak to trough (see Figure 5). We see possibilities for plateauing and trend reversal for shorter durations, but this cyclicality in the past indicates that in general, mortality trends are expected to continue to improve rather than deteriorate.

Some of the factors changing the pace of improvement affect multiple generations at once. For example, obesity is rising in all age groups in many advanced markets. Others, such as innovation in cancer screening or preventative medication often impact life expectancy from a certain point, with older groups experiencing less of the benefit. The majority of screening and vaccination efforts prioritise groups before they are diagnosed with a disease and treatments are often targeted towards earlier stages of a condition – these are all more likely to have a disproportionate benefit on the relatively younger groups.

Since 2010, the rate of mortality improvement in advanced countries such as the US, Canada and the UK has slowed sharply, primarily as initial improvements in CVD deaths have plateaued.[2] The length of the current slowdown is longer than typically seen in prior plateaus in the 20th century. Given the cyclical nature of improvements, we would expect to soon reach a tipping point and enter the next wave of rapid improvement.

The US is a special case as an advanced market in which, for certain recent periods, mortality improvement has been negative, i.e. life expectancy has declined. This originates from factors such as unequal access to healthcare, high opioid addiction and death rates, high societal obesity due to poor cardiometabolic health[3] and high levels of deaths from violent crimes, compared to other countries. However, most of these factors are not expected to apply to the same degree to the insured population.[4] The top socioeconomic deciles in the US generally experience higher mortality improvements than the overall population, though this is also on a declining trend. In addition, the policy choices and societal factors that are driving this divergence can be addressed in the long term.

2 *NCHS Data Visualization Gallery – Mortality Trends in the United States*, cdc.gov, 25 August 2020.
3 M. O'Hearn, et. al., "Trends and Disparities in Cardiometabolic Health Among U.S. Adults, 1999–2018", Journal of the American College of Cardiology, 2022.
4 L. A. Blewett et. al., "IPUMS Health Surveys: National Health Interview Survey, Version 7.2", 2022.

How does socioeconomic status affect mortality outcomes?
There is a broad understanding that there are variations in mortality trends when considering socioeconomic status measures such as education, income, occupation and wealth.[5] An individual's ability to access and benefit from healthcare or (private) L&H insurance is influenced by their socioeconomic status. Socioeconomic status is a major determinant of mortality risk in many mature markets, with the risk of dying inversely proportionate to income levels.[6] Large international studies have shown that individuals of lower socioeconomic status have greater premature mortality than those with high socioeconomic status. Low socioeconomic status is also associated with a 2.1-year reduction in life expectancy between the ages of 40–85.[7] For example, Figure 4 depicts the mortality attributable to socioeconomic inequality in England.[8]

Figure 4
Mortality attributable to socioeconomic inequality in England by sex, age and socioeconomic status (2003–2018, in five-year age cohorts).

Mortality attributable to socioeconomic inequality

■ –30% ■ –20% ■ –10% ☐ 0% ■ 10% ■ 20% ■ 30% ■ 40% ■ 50% ■ 60% ■ 70% ■ 80%
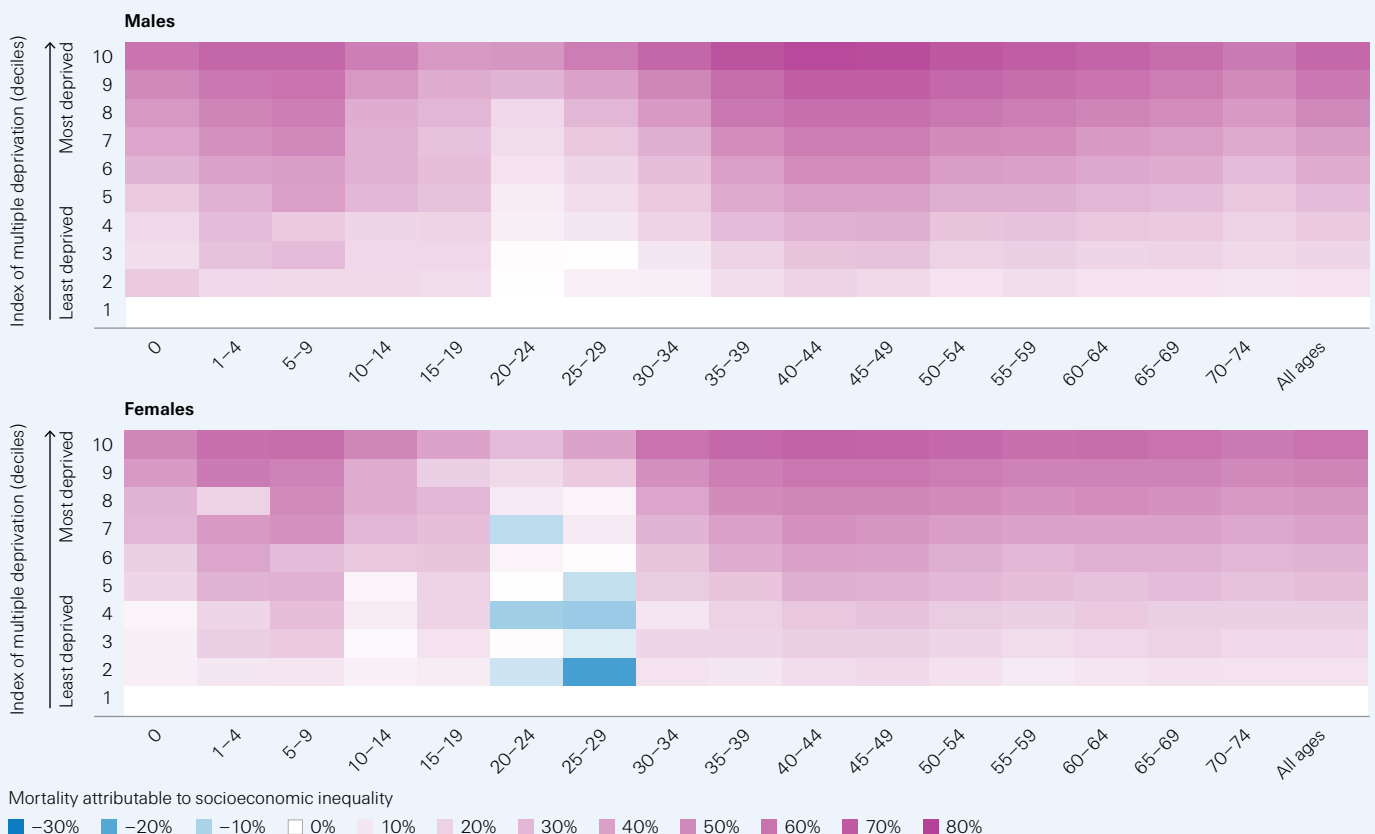
Source: D. Lewer et al., "Premature mortality attributable to socioeconomic inequality in England between 2003–2018: an observational study", *The Lancet Public Health*, 2019, reproduced by Swiss Re Institute

As life insurers' portfolio compositions change with time, population-level data offers a more stable benchmark across countries, socioeconomic groups and genders. Data unavailability and heterogeneity of insured population data typically drive mortality modellers to search for proxies in the general population data. Relying on aggregate population trends for the assessment of this group may lead to significantly more conservative estimates, since recent data indicates divergence in mortality trends for different sub-groups of the general population.

Mortality data for relevant socioeconomic deciles of the general population that match an insurer's portfolio composition is the best approximation of an insured book from which to forecast mortality improvements. However, in practice this is not a perfect proxy for the behaviour of insured lives, because the demographic mix and societal segments insured in each portfolio evolves by region, country and year. The impact of medical underwriting also differs between cohorts and products, and changes by policy duration.

5 D. Lewer et. al., "Premature mortality attributable to socioeconomic inequality in England between 2003 and 2018: an observational study", The Lancet Public Health, 2020.
6 P. Grigoriev et. al., "Socioeconomic differences in mortality among 27 million economically active Germans: a cross-sectional analysis of the German Pension Fund data", Socioeconomic differences in mortality among 27 million economically active Germans: a cross-sectional analysis of the German Pension Fund data, 2019.
7 S. Stringhini et. al., "Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women", The Lancet, 2017.
8 B. Bosworth, "Increasing Disparities in Mortality by Socioeconomic Status", Annual Review of Public Health, 2018.

Our research shows that three main factors should be considered as we analyse past trends in long term mortality improvement:

1) **Cyclicality:** what is the likely timeframe of trend changes (acceleration or reversal) in a country?
2) **Divergence:** could the US start to reverse and equalise the mortality experience across socioeconomic status, or might other countries start to see divergence too?
3) **Insured population dynamics:** higher socioeconomic groups offer a proxy for the insured population for near-term mortality improvement trends, but does this hold true for the long term?

Mortality improvements in advanced markets

Mortality improvements in advanced markets have historically outpaced those in developing countries (see Figure 5). We use Japan and Switzerland as examples of countries with the highest longevity. Both have benefited from good access to healthcare and management of lifestyle risk factors. The UK and the US are examples of large advanced markets with high life expectancies that face societal lifestyle-driven challenges, such as diabetes and obesity.

All life expectancy figures in this research are period life expectancies, split by age band and sex. These are calculated based on the mortality rates for a particular calendar year and, unlike cohort life expectancy, do not allow for future assumed changes in mortality rates.

Figure 4
Life expectancy by continent, 1900–2021
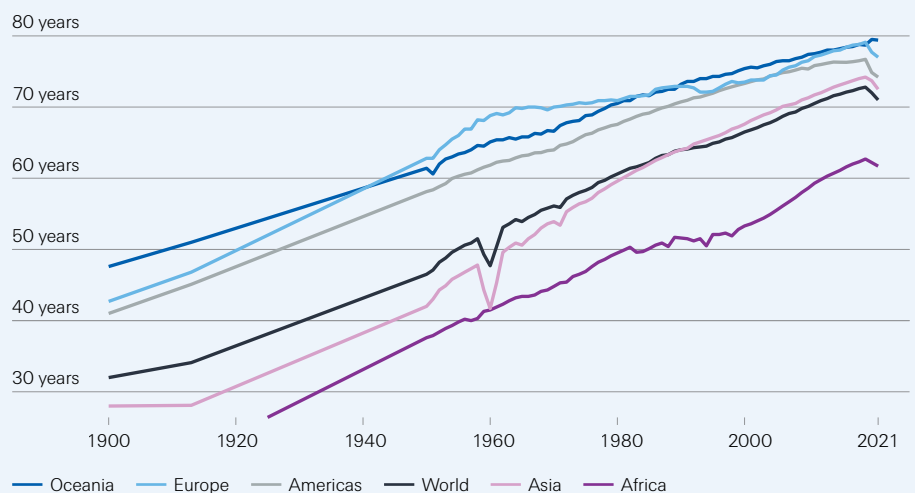
Source: various national agencies collated by Our World in Data – reproduced by Swiss Re Institute

Figure 5
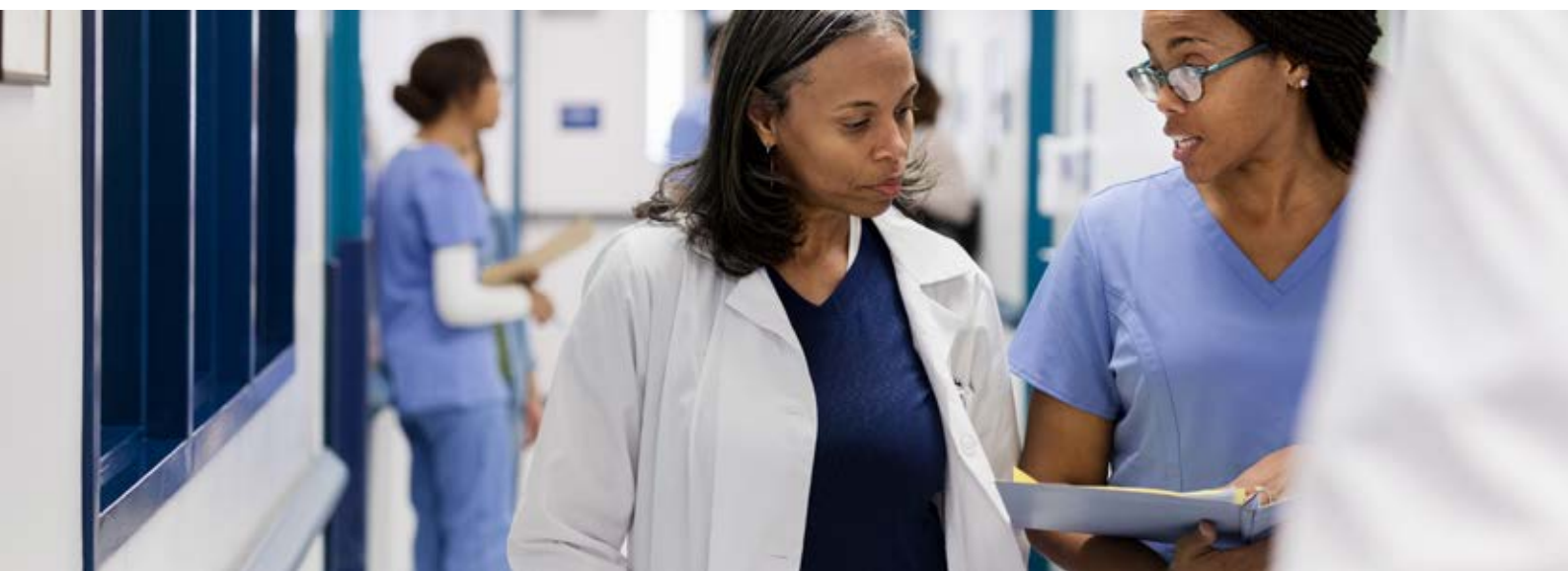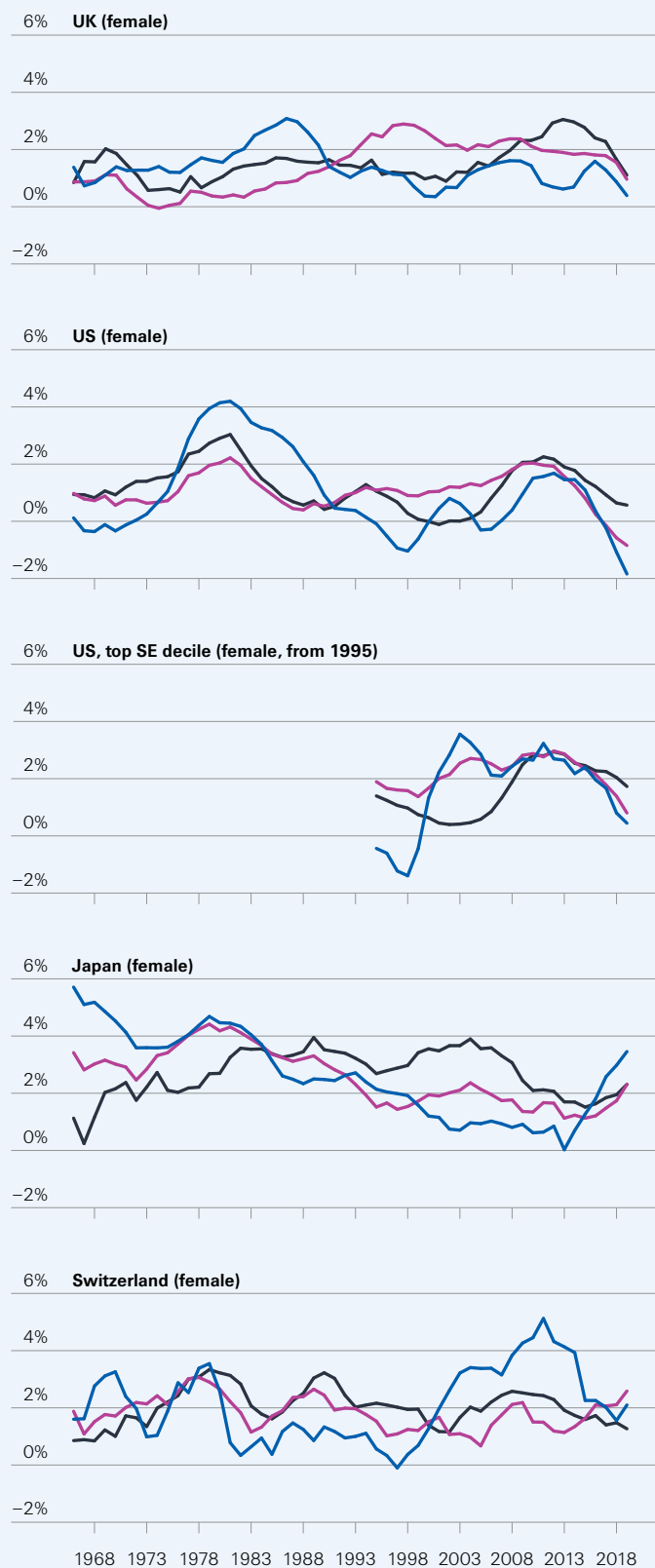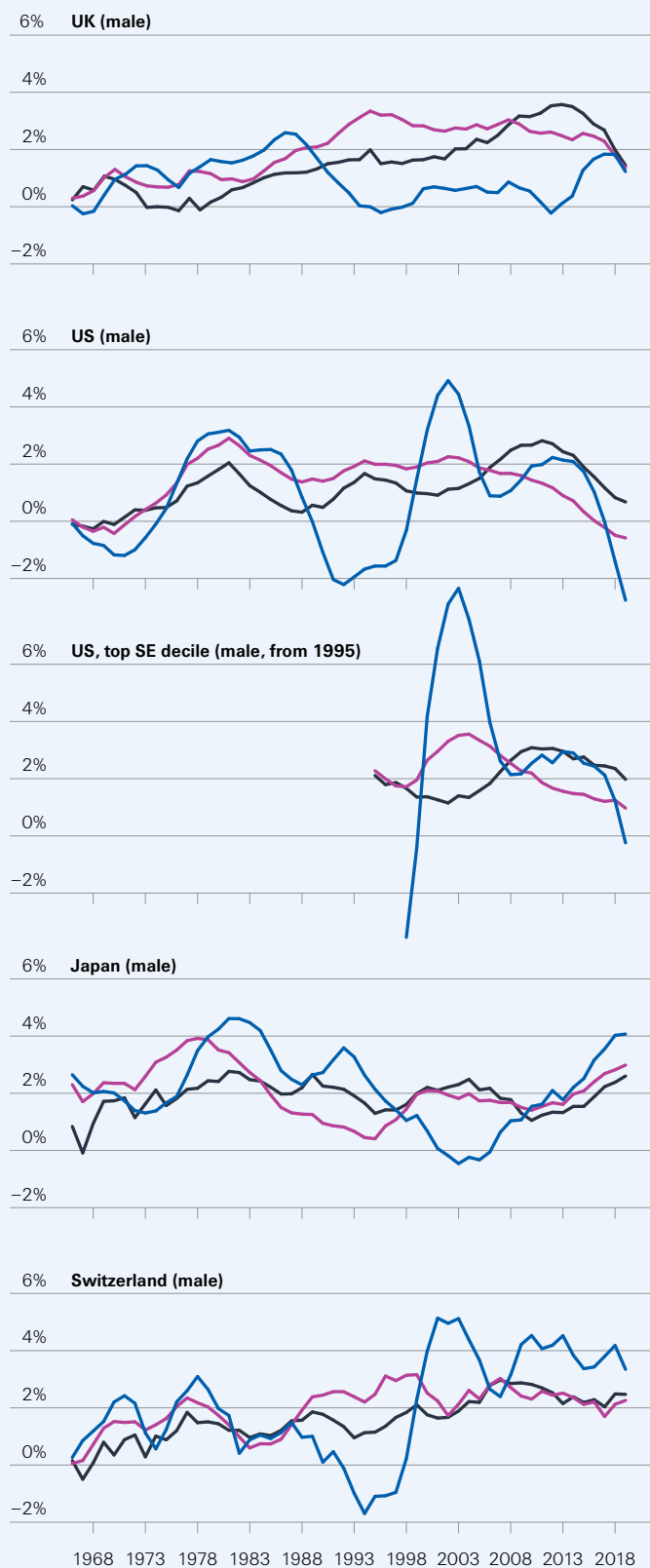Mortality improvement of males (left) and females (right) across select countries, 1966–2019

Mortality improvements, 8-year moving averages, female (1966–2019)

Mortality improvements, 8-year moving averages, male (1966–2019)

Age: —— 40 years   —— 60 years   —— 80 years

Age: —— 40 years   —— 60 years   —— 80 years

Source: Human Mortality Database (HMD) – analysed by Swiss Re Institute

The UK
The UK has experienced huge life expectancy gains since the 1960s, albeit with a clear peak and trough pattern (see Figure 5). About 70% of all mortality improvement between 1966 and 2010 is attributed to substantial reductions in circulatory disease-related deaths, followed by increasingly effective cancer treatments, and declining deaths from HIV and AIDS.

However, there has been a significant slowdown in mortality improvements since 2010. This flattening in the trend was created by a drop-off in mortality improvements from circulatory diseases, while cancer improvements remained comparable to the prior decade. In addition, conditions such as dementia and respiratory diseases contributed to higher mortality and therefore to reduced improvements.[9]

For males, the 1960s to early 1970s saw a negative mortality improvement across all age cohorts, most notably in the upper age bands (80-year-old males). The steepest improvement was seen in the 1970s and 1980s for those aged 50, who would have seen the greatest benefit from scientific and medical developments; including an awareness of dietary risk factors and the importance of healthier lifestyles, alongside the prescription of CVD drugs, both of which started to be widely adopted at the time. The rate of improvement slowed for males in age groups 60+ from the early 1980s. And from a peak around the mid-1980s, the male 50-year-old group also saw a rapid decline in improvements, attributable to fewer medical advancements. This only began to recover in the early 2000s, before reaching the 2010 plateau.

The US
The US trajectory for mortality improvements has negatively diverged away from other advanced countries, faring far worse than other Organization for Economic Co-operation and Development (OECD) nations (see Figure 5). The US experienced slower mortality improvement than other OECD nations even before the broad global plateau in improvement from 2010. Only the top 10% of the US population by socioeconomic status had comparable life expectancy at birth to the OECD average, as of 2019. Even the wealthiest segments of the female US population live less long than an average woman in Japan.

Many countries have some disparity in life expectancy between the highest and lowest socioeconomic deciles, but in the US this gap is large, has increased significantly since the 1980s, and there is an expectation that this divergence will continue in the near to medium term.[10] Outcomes for lower socioeconomic groups have deteriorated sharply

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[9]   J. Palin, "Mortality improvements in decline", TheActuary.com, August 2017.
[10] M. Barbieri, "Mortality by Socioeconomic Category in the United States", Society of Actuaries, 2022.

due to factors including deaths of despair (alcohol and drug overdoses, suicides), lack of access to healthcare, and violent deaths.

Though mortality improvements in higher socioeconomic groups in the US have held up better, they are also declining. The drivers are likely to be a combination of varying employment rates and the prospect of financial instability, routinely consuming less nutritious foods, and access to and affordability of healthcare, among others. Without societal change, we would expect this trend to continue for the next several decades, although the magnitude of the disparity may alter with trend changes.

A 2020 US Society of Actuaries (SOA) study categorises US counties based on a socioeconomic score and then splits them into deciles.[11] Studies of demographic factors are relatively common, especially around race or regional variation, but comparatively little attention has been paid to socioeconomic scores. By splitting the US population into deciles by ranked county socioeconomic scores, the study found:
- In general, each more affluent decile had a greater life expectancy than the one below it.
- The median three deciles (4−6) would occasionally overlap in some years but return to a hierarchical top-to-bottom life expectancy in other periods.
- In 2019, the difference in life expectancy between the highest and lowest decile was 7.2 years for men and 5.7 years for women.
- The difference in life expectancy between the two extreme deciles rose steadily over the decades. This was likely driven by deterioration in the health status of individuals in the lowest decile, and possibly also an acceleration in improvement in the survival odds of the highest decile population.

As a result, a reliance on US population trends may lead to a significantly more conservative estimate of mortality improvement, as an insured population belonging to higher socioeconomic groups may diverge positively from the general population.

Longevity champions: Japan and Switzerland

Japan and Switzerland are two countries that have among the highest life expectancies in the world.[12] A combination of lifestyle factors and healthcare advancements, including access to high quality healthcare, have led to better overall health profiles for the average person. While the Swiss are a model for the importance of physical activity and exercise, the Japanese identified and addressed key country-specific, population-level risk factors such as diet. Both countries present interesting case studies of potential paths to accelerate longevity at the population level.

Japan
Japan today leads the G7 in population life expectancy primarily due to stunning improvements in CVD survival rates. The country has achieved rapid improvements in mortality rates from the 1960s, when deaths from cerebrovascular disease and stomach cancer led to very poor life expectancies.

Today's much lower premature mortality rates are also attributed to higher survivability of ischaemic heart disease, and breast and prostate cancers.[13] These mortality improvements are due to a huge extension of post-war lifespans from diet and healthcare advances. However, Japan reached its plateau in improvement much earlier than other advanced markets (2006–2011), followed by an acceleration in improvements.[14]

[11] M. Barbieri, "Mortality by Socioeconomic Category in the United States" (2020 report), Society of Actuaries, December 2020.
[12] M. Roser et. al., "Life Expectancy", ourworldindata.org, October 2019.
[13] S. Tsugane, "Why has Japan become the world's most long-lived country: insights from a food and nutrition perspective", European Journal of Clinical Nutrition, 2021.
[14] *Changing trends in mortality: an international comparison: 2000 to 2016*, ons.gov.uk, August 2018.

Historically, the two leading causes of death were CVD-related conditions, primarily ischaemic heart disease and stroke. Strong regulatory interventions and public awareness of health led to declines in age-adjusted mortality rates from these causes of 61% and 83% respectively among 35–84-year-olds, between 1980 and 2012. Japan took decisive public health action much sooner than other comparable countries and has already met many of the easier goals to reduce mortality. This healthier population is forecast to see a 16.5% decline in chronic heart disease and stroke deaths between 2011–2030. The limited room for improvement is clearer when compared to countries such as the US (27% forecast decline) and the UK (56%).[15]

Projections of male and female life expectancy at birth continue to increase steadily for people born between 2015 and 2065. This is a consequence of medical advancements in cancer and better treatments for neurodegenerative diseases, all alongside the promotion of healthier lifestyles.[16] Japan is already one of the oldest nations in the world, with 29.1% of people over the age of 65.

Recent years show that the extension of lifespans shows no sign of abating, and Japan is expected to continue to set the benchmark for longevity. The longevity of its centenarians in particular is likely to inform global views on maximum lifespans and where assumptions for the "omega" or maximum age for the rest of the world should be set.

Switzerland

Like Japan, Switzerland is a leader for life expectancy, at 84 years.[17] Not only that, the average health status is one of the highest of all OECD countries. The 50+ age cohorts of Swiss males have experienced significant mortality improvements since the early 1960s (see Figure 5). The greatest have been in the 50-year-old cohort, which have seen continued increases with fewer troughs, driven, as elsewhere, by reduced premature CVD mortality.

Switzerland's healthcare system is expensive but well-funded with low wait times and broad access to a range of specialists in different medical settings. Universal access to healthcare, alongside a strong system of preventative medicine, means that many medical problems are identified early.

A strong culture of outdoor, physical activity and nutrition focused on natural whole foods, with lower uptake of ultra-processed foods, has led to some of the lowest obesity rates in the developed world. Although Switzerland has seen an increase in obesity rates in recent years, there is evidence that these are stabilising[18]. Either way, it remains less obese than many other countries, especially as an advanced market, making the Swiss one of the healthiest populations globally- and a case study on how lifestyle choices and health policy can extend not just lifespans but to help us live longer, healthier lives.

[15] E. Kiyoshige, et. al., "Projections of future coronary heart disease and stroke mortality in Japan until 2040: a Bayesian age-period-cohort analysis", The Lancet Regional Health Western Pacific, 2023.
[16] *Country report – Japan*, actuaries.org, November 2018.
[17] *Trends in life expectancy – Health at a Glance 2021*: OECD Indicators, 2021. oecd-ilibrary.org.
[18] *Swiss Health Survey 2017: overweight and obesity. Proportion of overweight people in the population has stabilised*, bfs.admin.ch, 2020.

Tracking COVID-19 mortality and its impact
Given the distortion that COVID-19 impacts add to mortality data, our historic analyses in this report use data up to 2019. The excess deaths resulting directly or indirectly from the pandemic should appropriately be excluded from any analysis for developing base mortality rates or future long-term mortality trends.

Global deaths from all causes – COVID-19 and others – increased far beyond expected levels in 2020–2022. The US Centers for Disease Control and Prevention (CDC) cause of death reporting illustrates this well, when comparing 2020–2022 to the previous 5-year average (see Figure 6). The only two conditions that did not follow this pattern were cancer, which remained broadly consistent throughout the three years, and respiratory diseases.

Diabetes, and Alzheimer's & dementia, are diseases where there is little seasonality in death. Yet they averaged an increase of 13% and 23% respectively over the three years of the pandemic. Likewise, circulatory diseases were elevated almost 13% during the pandemic, while cancer were only 1% higher than average.

Diabetes, Alzheimer's disease and circulatory disease are all highly correlated with older ages and higher levels of obesity and other markers of metabolic ill health, all factors that are highly predictive of poor COVID-19 survival. The likely reason for this substantial increase in reported deaths due to these conditions is that these were COVID-19 related conditions that were to a large extent misreported as other causes of death.

Figure 6
US cause of death, split by disease type. There was a substantial increase in deaths that were likely misattributed as non-COVID-19 deaths

■ Alzheimer's & dementia ■ Circulatory diseases ■ Cancer ■ Respiratory diseases ■ Diabetes
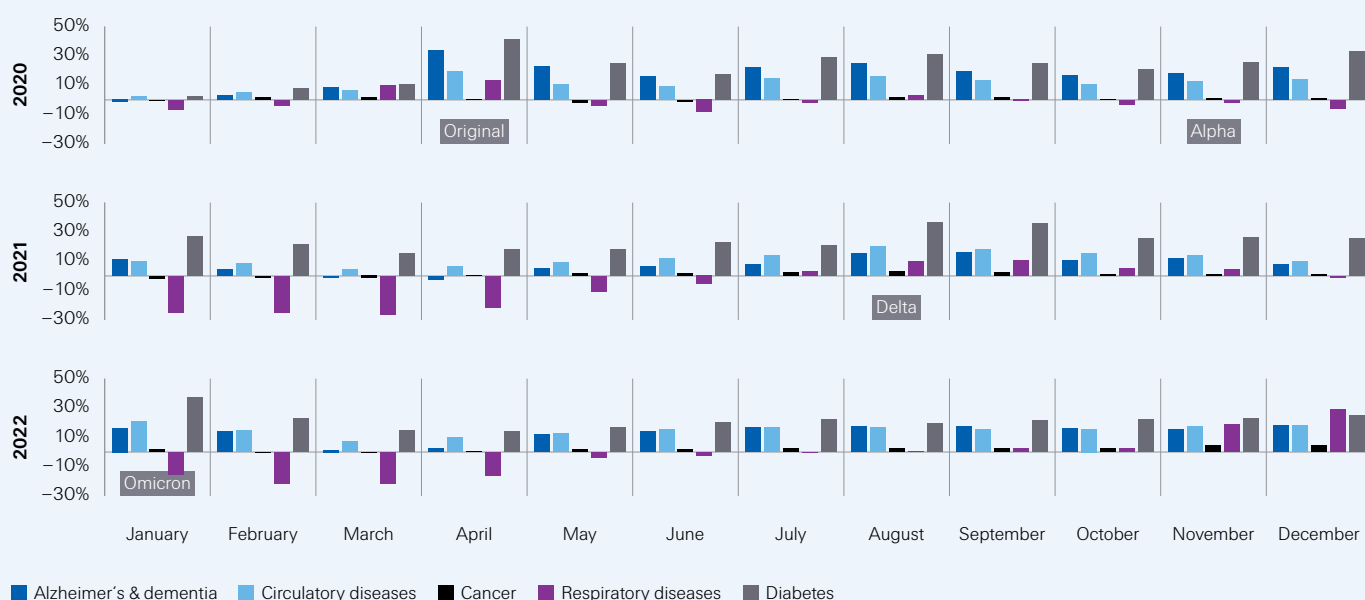
Source: US Centers for Disease Control and Prevention (CDC) – analysed by Swiss Re Institute

Though many countries are well past the peaks of their pandemic, it can nevertheless be expected that COVID-19 will continue to lead to some level of mortality. We are likely to see some element of seasonality, with waves of COVID-19 leading to ongoing deaths – in the same way that the 1918 influenza (Spanish flu) seeded annual seasonal influenza pandemics for at least a century after.

COVID-19 is a multi-system disease that can affect every organ. In the longer term, alongside future acute COVID-19 waves, is the potential impact of long-term sequelae of COVID-19 (Long COVID), whether or not a person tested positive for COVID-19 or had a symptomatic infection. Some reports suggest that for patients experiencing Long Covid, symptoms can abate within several months to perhaps a year or more[19], but others may linger for far longer, and there is yet uncertainty around whether some of these will resolve. New research continues to shed light on this topic, but it may be a number of years before the true impact of Long COVID is understood.

Even given these uncertainties, a mean reversion of mortality levels and mortality trends is likely once the effect of the pandemic abates. COVID years are therefore excluded from the data analysis.

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[19] S. W. Hanson, et. al., "Estimated Global Proportions of Individuals With Persistent Fatigue, Cognitive, and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2021", JAMA, 2022.

Major causes of death trends and medical advancements

- **Cancer mortality is expected to see the greatest magnitude of improvements.** We expect better and more personalised treatments, screening and diagnostics to drive cancer mortality improvements for the next 25 years or more.
- **CVD improvements are approaching a saturation point** after vast gains in past decades. Further improvement will rely on societal, policy and behavioural changes such as addressing diabetes and obesity via better nutrition and physical activity.
- **Ageing diseases will likely benefit from improvement over the next 20+ years,** as these diseases suffer from a substantial gap in knowledge and ready treatments today.
- **We focus on factors with a relatively high degree of plausibility.** We are aware that as-yet unknown technologies, diseases or socio-political change could impact future mortality rates, but due to the level of uncertainty we do not attempt to examine these.

Advancements in technology, medical sciences and public health policy have accelerated in the past 20 years. This has brought vast improvement in the prevention, diagnosis and treatment of diseases, and increased lifespans at every age.

A forward-looking analysis of drivers of improvement relies upon identifying the sources of future longevity gains from medical innovations. Medical advancements may originate from early-stage technologies, those close to being widely deployed, and many more research breakthroughs and technological developments that are as yet unknown. We offer a directional vector that includes key potential breakthroughs today, and reasonable trajectories that the science may take in the future.

Figure 7
Future medical innovations likely to drive mortality improvements
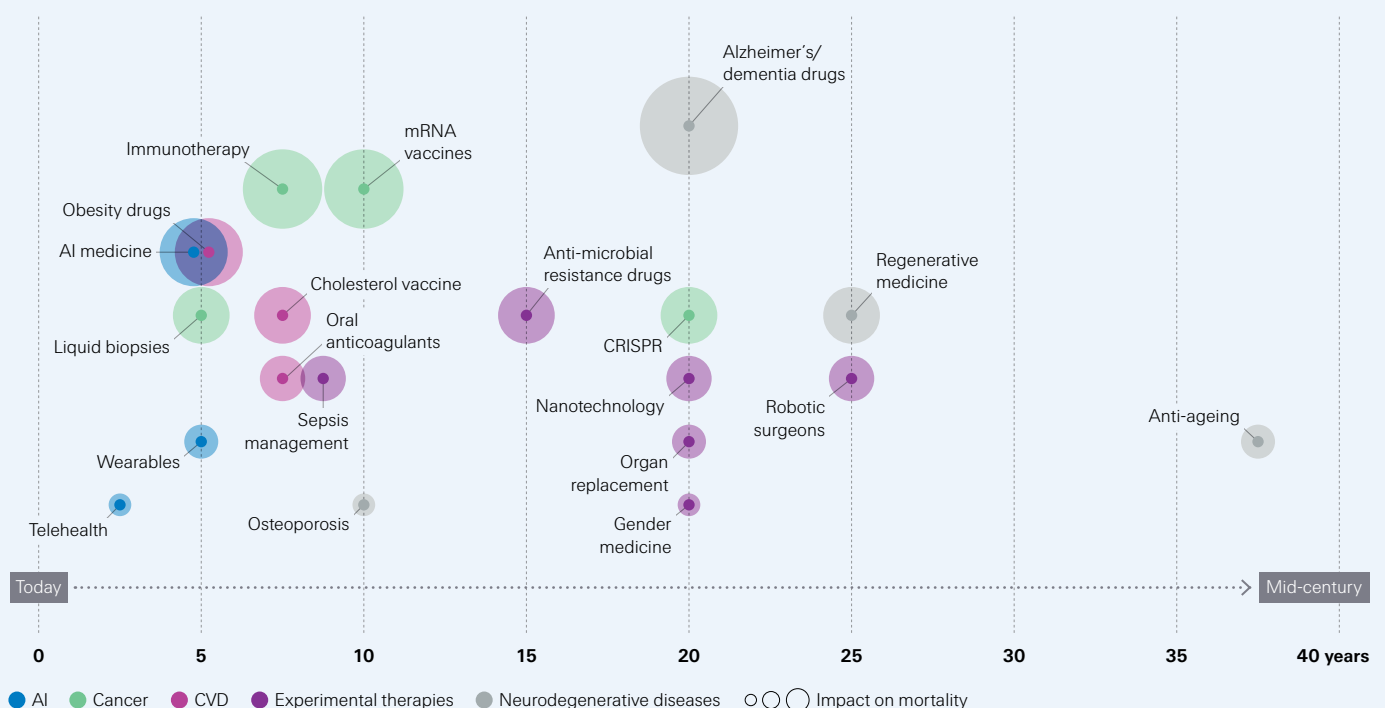
Source: Swiss Re Institute

We see three trends likely to drive the next waves of mortality improvements:
- accelerating gains in cancer-related mortality due to better diagnostics and treatment;
- potential for incremental improvement in CVD deaths primarily through lifestyle and behaviour modifications; and
- steady improvement in ageing-related and neurodegenerative diseases such as Alzheimer's over a longer time horizon.

Cancer

Cancer causes about 10 million deaths worldwide each year, or one in every six deaths.[20] Incidence is increasing in absolute terms globally, primarily driven by population ageing. However, so are survival rates, albeit varying by cancer type and diagnosis timeframes.[21] Cancer mortality improvement in past decades has been driven by smoking cessation and the introduction of large-scale national screening programmes for certain cancer types.

We expect ongoing cancer mortality improvements over the next 20 years. Smaller but continued improvements are expected in later decades, by saturation or balance of therapy advancements and behaviour/risk factor improvements.

We see two key advancements supporting cancer mortality improvements over the next 30 years:

- **the evolution of diagnostics** to AI-driven multi-cancer diagnostic technologies, use of novel cancer biomarkers, and more personalised screening, and
- **the shift to personalised medicine** such as immunotherapy, targeted treatments and gene therapy.

Cancer survival rates are being improved by earlier diagnosis due to better screening programmes. For example, the UK offers public screening for breast, cervical, and colorectal cancers, and uptake is relatively high, leading to higher survival rates with earlier detection. Later diagnoses are often associated with poorer mortality outcomes. Ovarian (54% 5-year survival rate), pancreatic (51%) and non-Hodgkin lymphoma (58%) are more commonly diagnosed at an advanced stage.[22] These harder-to detect and difficult-to-treat cancers have seen little progress in recent years. For example, pancreatic cancer's five-year survival rate is largely unchanged since the 1960s due to delayed detection and the inherent aggressive tumour biology.

As diagnostics and targeted drug delivery improves, we expect early detection to lead to higher survival rates. As technology improves and treatment shifts from symptom-based treatment to precision medicine (see section below) we see potential for major further improvements. Older age groups, likely those aged 60–80 years, may benefit most from new precision oncology therapies and screening innovations.

Even with these developments, we do not yet see advances in the horizon for hard-to-detect cancers, as well as solid tumours (pancreatic, liver) and haematologic (blood – leukaemia) cancers. The time horizon for medical solutions to these may well extend beyond 40 years.

If and when these technologies become available, they are likelyto be very expensive and difficult to access. These potentially high costs will need to considered alongside eligibility and the assumed benefits to patients.As time progresses, these costs will likely decrease, through further technological progress and economies of scale, opening the newer medical options to a wider group of patients.

[20] Cancer, who.int, February 2022.
[21] Estimated number of new cases from 2020 to 2040, Males and Females, age [0−85+], gco.iarc.fr/tomorrow, 2023.
[22] Cancer survival statistics, cancerresearchuk.org, accessed May 2023.

Future cancer advancements

The evolution of diagnostics
Cancer screening and detection is evolving from invasive and painful tissue biopsies to blood test-based "liquid biopsies" that can quickly and painlessly provide the genetic material to identify and profile cancers. By detecting cancer-derived components circulating in the blood, liquid biopsies offer much earlier-stage cancer screening than a tissue biopsy after a tumour is identified.

Liquid biopsies detect cancer components including circulating tumour cells (CTC) and tumour DNA (ctDNA) or cell-free DNA (cf-DNA) and RNA that can serve as biomarkers of disease. As such, they enable doctors to confirm a cancer diagnosis very early and identify genetic alterations that could guide personalised and targeted treatment plans. Recent studies indicate that monitoring ctDNA can detect cancer relapse before CT imaging, highlighting its value for early-stage screening, especially for high-risk individuals.

Liquid biopsies can provide a more complete profile of a patient's cancer (crucial for tailored drug therapies) than tissue-based sequencing, which could provide an incomplete tumour profile, if only small samples are taken which could not account for tumour heterogeneity. Serial sampling allows for profiling of tumours that are inaccessible by tissue biopsy, for tracking disease progression and to determine the efficacy of cancer treatment in real time.

At the present time, as an earlier-stage test, liquid biopsies can be less sensitive and specific than tissue biopsies. This can mean a higher occurrence of false positive and false negative results. Recent studies reported 67% sensitivity for detecting 12 cancers that account for about two-thirds of annual US cancer deaths, and 44% sensitivity for detecting all tested cancer types. We expect the predictive power of these tests to improve over time.[23]
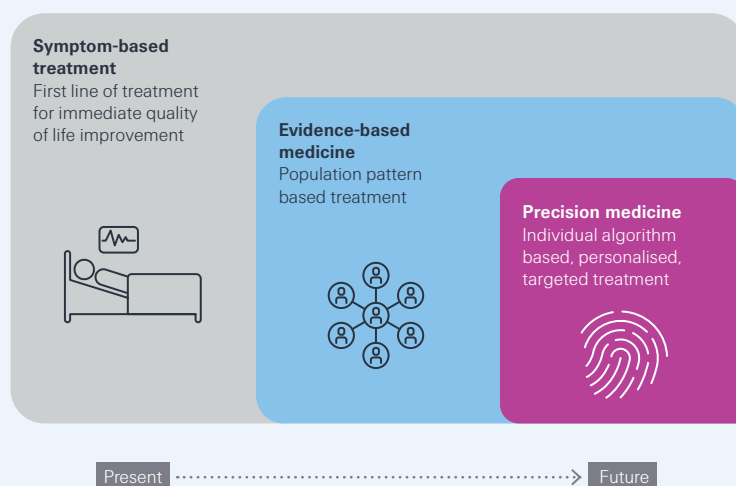
The shift to personalised medicine
Healthcare was historically based on trying to alleviate a patient's symptoms without considering the underlying cause (or "aetiology") of the condition. This progressed to evidence-based medicine that seeks to treat the underlying causes of disease, and has

[23] S. H. Gawel, et. al., "Current and future opportunities for liquid biopsy of circulating biomarkers to aid in early cancer detection", Journal of Cancer Metastasis and Treatment, 2022.

Figure 8
The evolving trajectory of healthcare approaches

Symptom-based treatment
First line of treatment for immediate quality of life improvement

Evidence-based medicine
Population pattern based treatment

Precision medicine
Individual algorithm based, personalised, targeted treatment

Present ·····························> Future

Source: Swiss Re Institute

resulted in many conditions, especially cancer, becoming far more survivable than they previously used to be. We are now on the precipice of precision medicine – a personalised approach that takes our previous learnings and tailors a patient's treatment for their specific condition (see Figure 8).

An early example of this are the first-in-class drugs targeting the immune system, such as a combination of nivolumab/relatlimab, which have proven to be successful in treating later stage melanomas. This drug combination empowers the immune system to destroy tumours, while limiting the cancer's ability to resist an immune system attack.

Aside from the obvious treatment benefits from this, we could expect improvements in treatment efficacy and fewer adverse effects. This could lead to lower morbidity and mortality, and a reduction in inefficient, time consuming and expensive treatments.

Short-term benefits are likely to come from early diagnoses and the optimised use of existing targeted therapies, such as monoclonal antibodies, for widely treated cancers. Longer-term benefits likely come from an even more personalised medicine approach driven by gene editing and priming one's own system to fight the disease (CRISPR, T-cell strategies, among others). However, personalised medicine may be expensive and time-consuming to implement in the early years.

Personalised cancer therapies
There are two key avenues for personalised medicine in cancer therapies:

mRNA therapies: in a deceptively simple way, an mRNA vaccine unleashes a patient's immune system against a cancer tumour.[24] The therapy creates a personalised vaccine from a patient's cancer cells to enable the patient's own immune system to attack the cancer.[25] Soon after diagnosis, a biopsy of the tumour is analysed to identify DNA mutations only found in the cancerous cells.[26] Once found, these proteins, termed "tumour-associated antigens", become the perfect target for treatment. Since they are only present on the surface of cancer cells, any cells displaying them must be cancerous. The immune system destroys only the cells displaying these neoantigens and leaves healthy cells untouched.

The highly specific nature of this technology, based on the individualised identification of cancer mutations and the underlying biology of a patient's cancer, means it has the potential to treat all patients, regardless of cancer type. Clinical trials are often limited in scope, but the outcomes appear very promising.[27] However, despite decades of research, to date no mRNA-based cancer vaccine has been approved by the US FDA or other regulatory bodies. It is hoped that the success of mRNA vaccines for COVID-19 could help to accelerate research into cancer vaccines. Success will also rely on rapid manufacturing of the vaccine, to make it available within weeks of the biopsy.

T-cell strategies: also known as chimeric antigen receptor or CAR T-cells therapy, these similarly use a person's own immune system to recognise and fight cancer. T-cells, which are a part of the body's immune system, are taken from a patient's blood and modified in a lab by adding a gene (a chimeric antigen receptor) that helps the T-cells to attach to a cancer cell antigen. Since different cancers have different antigens, each CAR is made for a specific cancer's antigen. The CAR T-cells are transferred back to the patient where they act as a "living drug" by destroying cancer cells through several mechanisms.[28,29] CAR T-cell therapy is available for specific kinds of lymphomas and leukaemias, as well as multiple myeloma, but several hundreds of clinical trials are in place for other cancer types. Solid tumours have been challenging because it is difficult to identify target antigens on the surface of solid tumours but not on healthy/ non-cancerous cells.

[24] Q. He et. al., "mRNA cancer vaccines: Advances, trends and challenges", Acta Pharmaceutica Sinica B, 2022.
[25] C. Lund Lorentzen et.al., "Clinical advances and ongoing trials of mRNA vaccines for cancer treatment", The Lancet Oncology, 2022.
[26] E. Winstead, "Can mRNA Vaccines Help Treat Cancer?", cancer.gov, 2022.
[27] Moderna and Merck Announce mRNA-4157/V940, an Investigational Personalized mRNA Cancer Vaccine, in Combination with KEYTRUDA(R) (pembrolizumab), Met Primary Efficacy Endpoint in Phase 2b KEYNOTE-942 Trial, investors.modernatx.com, 2022.
[28] CAR T-cell therapy, cancerresearchuk.org, accessed May 2023.
[29] CAR T-cell Therapy and Its Side Effects, American Cancer Society, accessed May 2023.

CAR T-cell therapy is not routinely offered to most cancer patients until they have exhausted other treatment options, but this will likely change as the technology becomes less expensive and faster to implement. Two recent large studies showed CAR T-cell therapy to be more effective than current standard treatments for patients with non-Hodgkin lymphoma whose cancer returned after initial chemotherapy. These results could lead to a change in clinical practice, with CAR T-cell therapies being used earlier against lymphomas and other cancers, to potentially improve survival rates.[30]

Cardiovascular diseases

CVD are defined as heart attacks (myocardial infarction), stroke and ischaemic heart disease, and is a leading cause of mortality and morbidity in both general and insured populations globally. After vast CVD mortality improvements in past decades, experts expect fewer gains going forward. Improvements are more likely to come from positive lifestyle changes as opposed to medical interventions.

Figure 9

US age-adjusted mortality rates by major causes of death
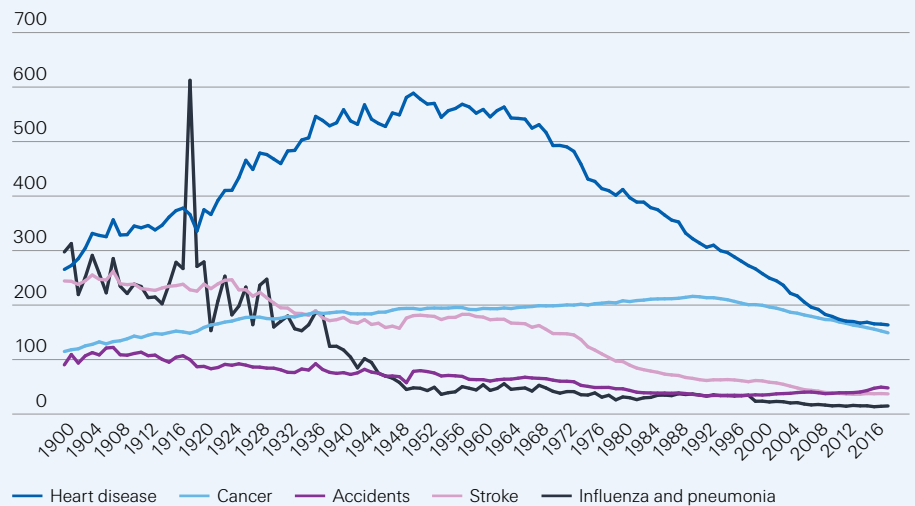
Source: US CDC – reproduced by Swiss Re Institute

In the UK, mortality from all CVD, stroke, and coronary heart disease declined by 70%, 71% and 72% respectively from 1979 to 2013.[31] The US also saw a 70% drop in heart disease-related deaths from 1968 to 2017, to 62 deaths per 100 000 people.[32]

The continued poor cardiovascular health of the US population has been a major headwind since 2010. Some new studies project a sharp rise in rates of CVD risk factors from 2025–2060. This includes expected increases of 40% in diabetes, 30% in dyslipidaemia, 25% in hypertension and 20% in obesity. This could lead to an increase in cardiovascular death if left unaddressed.

The management of underlying risk factors and prevention will therefore likely be the most important components to additional CVD mortality improvements. Progress in improving cardiovascular health may be impeded by unhealthy lifestyles, increasing obesity, uptake of smoking if e-cigarettes act as a gateway, increasing poverty and socioeconomic inequality, decreasing education levels, and increasing air pollution.

Unlike cancer, few countries have formalised, comprehensive CVD screening programmes, so there is greater reliance on individual actions to reduce risk. A move to

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30 Should CAR T Cells Be Used Earlier in People with Non-Hodgkin Lymphoma?, cancer.gov, 2022.
31 P. Bhatnagar, et. al., "Trends in the epidemiology of cardiovascular disease in the UK", Heart, 2016.
32 M. D. Ritchey, et al., "US trends in premature heart disease mortality over the past 50 years: Where do we go from here?", Trends Cardiovasc Med, 2020.

remote health monitoring may lead to fewer diagnosis opportunities. National screening programmes for heart disease or stroke risk would likely help to minimise cardiac events by identifying those at highest risk, and minimising likelihood of severe events by treating at an earlier timepoint.

Future pharmacological therapies could be developed to optimise existing offerings, incorporate newer technologies such as wearables, and address medication compliance in patient populations.

Future CVD advancements

The rollout of lipid-lowering **statins** to manage cholesterol since the 1980s significantly reduced the risk of cardiovascular events and potentially fatal heart attacks and strokes in those with coronary heart disease.[33]

Future drug development is focusing on other receptors and inhibitors as therapeutic targets for controlling cholesterol – such as the PCSK-9 protein, high levels of which have been shown to prevent liver breakdown of cholesterol, thereby increasing the risk of developing heart disease.[34] Two FDA approved monoclonal antibody drugs have demonstrated a reduction in low density lipoprotein cholesterol (LDL-C) through action on PCSK9 protein. When combined with a statin, these PCSK9 inhibitors have been shown to lower LDL cholesterol by up to 60%[35] and can significantly reduce the risk of myocardial infarction (MI), ischaemic stroke, and need for coronary revascularisation.[36]

Further drug development resulted in the creation of inclisiran – a synthetic molecule that has been heralded as a potential game changer in the treatment of high cholesterol. Inclisarin works on the PCSK9 gene and increasing LDL-C receptors, which in turn reduce levels of LDL-C. The drug comes with added benefit of a long biological half-life, only requiring bi-annual injectable dose.[37]

Despite being in the early stages of limited FDA approval and currently used alongside existing therapies, this drug has the potential to serve as an **anti-cholesterol 'vaccine'**. When administered by general practitioners or family doctors, there is the possibility of mitigating the patient compliance issues often associated with statins and monoclonal antibody treatments.[38]

[33] Should I take a statin?, bhf.org.uk, accessed May 2023.
[34] R. Chaudhary, et. al., "PCSK9 inhibitors: A new era of lipid lowering therapy", World Journal of Cardiology, 2017.
[35] J. R. Burnett & A. J. Hooper, "PCSK9 – A Journey to Cardiovascular Outcomes", NEJM, 2018.
[36] P. Guedeney et. al., "Efficacy and safety of alirocumab and evolocumab: a systematic review and meta-analysis of randomized controlled trials", European Heart Journal, 2022.
[37] New heart disease drug to be made available to NHS patients through ground-breaking collaboration, ox.ac.uk, 2020.
[38] R. O'Hare, "'Cholesterol vaccine': Twice-yearly jab could help to halve 'bad' cholesterol", imperial.ac.uk, 2018.
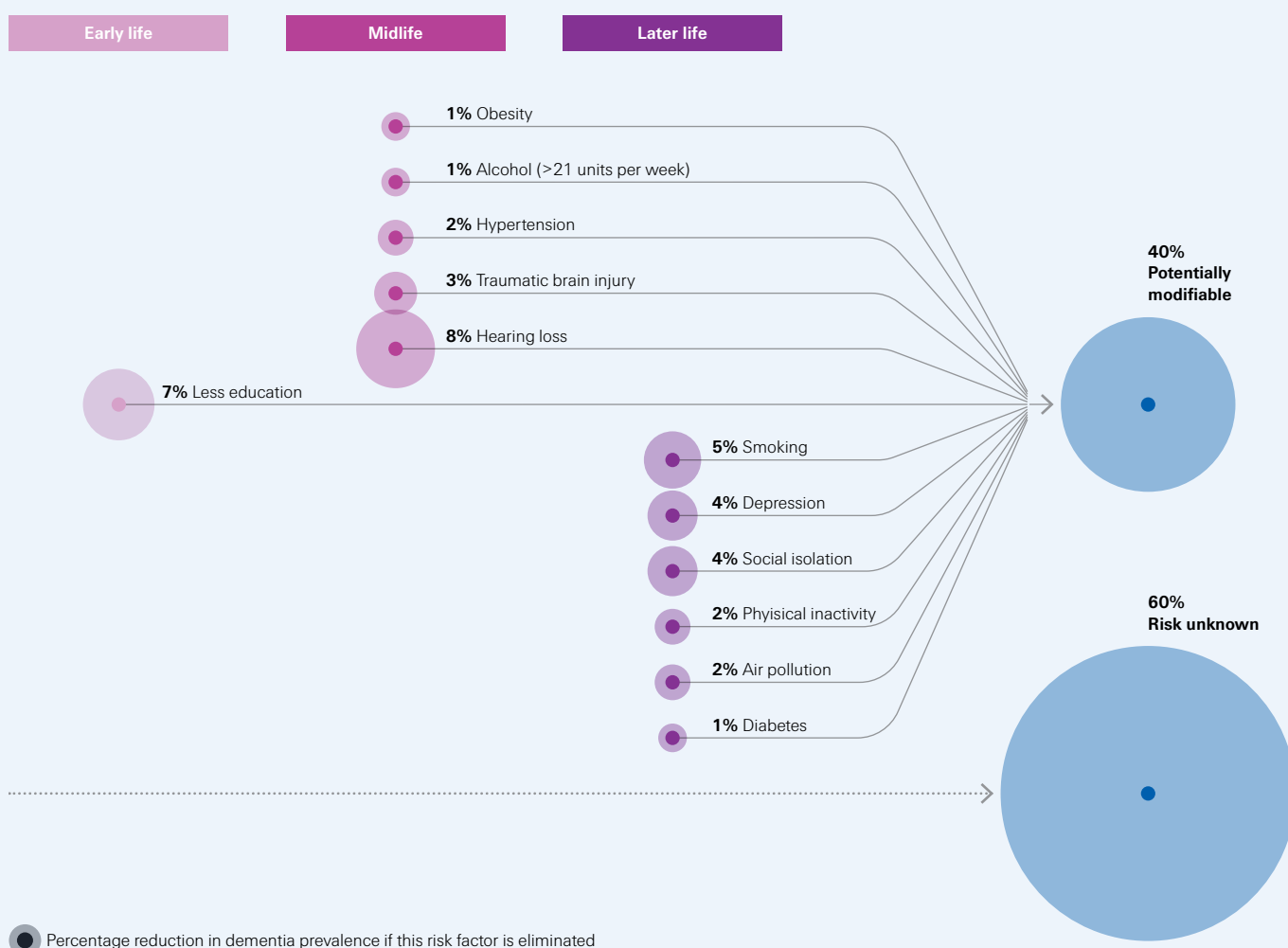
Ageing and neurodegenerative diseases

Ageing is defined as a progressive state marked by functional decline and the emergence of chronic age-related comorbidities. While mortality improvements are expected to continue, research has indicated that there may be a natural ceiling to age, correlated with a loss of physiological resilience between the ages of 120–150 years.[39] Gerontologists predict that the world's centenarian population will increase eightfold by 2050, but ageing is considered quite malleable, with the potential for biological ages much lower than chronological age.

However, many risk factors for ageing are mutually reinforcing and multiply over a lifetime. Ageing brings with it often irreparable bodily wear and tear, with symptomatic relief as the only solution. Ageing is the main risk factor for neurodegenerative diseases (NDDs) such as Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (motor neurone disease), which are progressive conditions leading to increased disability from loss of cognitive and/or motor function.[40]

[39] T. V. Pyrkov, et. al., "Longitudinal analysis of blood markers reveals progressive loss of resilience and predicts human lifespan limit", Nature Communications, 2021.
[40] K. Mayne, et. al., "Aging and Neurodegenerative Disease: Is the Adaptive Immune System a Friend or Foe?", Frontiers in Aging Neuroscience, 2020.

Figure 10
Risk factors for ageing

Percentage reduction in dementia prevalence if this risk factor is eliminated

Source: G. Livingstone et al., *Dementia prevention, intervention, and care: 2020 report of the Lancet Commission*, reproduced by Swiss Re Institute

Alzheimer's disease and dementia

One key NDD is Alzheimer's disease – a progressive, multifactorial neurodegenerative disorder characterised by a gradual loss of functional, behavioural and cognitive abilities. Alzheimer's is the most common cause of dementia, contributing to 60–80% of cases.[41] Dementia is a generalised term for impaired thinking and memory loss. This impairment is severe enough to be labelled as a symptom, and is not a usual part of ageing, or synonymous with the gradual decline in executive function commonly reported in older age groups. The risk factors of dementia are varied, with 40% falling into the range of being potentially modifiable behaviours and activities throughout life (see Figure 10). The remaining 60% of the risk remains unknown, likely comprising genetic factors, as yet unidentified lifestyle factors and other determinants.[42] Higher incidence in future could be influenced by a growing proportion of people with a high BMI leading to Type 2 diabetes, along with air pollutants and consumption of processed foods.

The expected trajectory of mortality from neurodegenerative disorders (NDD) is very uncertain. Reported NDD mortality has increased (rising by 148% globally from 1990 to 2019).[43] Given increased clinical recognition and formal diagnoses of NDD in the ageing population, they are becoming more common as a cause of death on death certificates. It is unclear whether this represents a real increase in deaths from NDD, or is a consequence of patients dying with an NDD rather than of the condition.

There are no widely accessible screening programmes for Alzheimer's disease unless an individual presents with a family history and genetic predisposition to the disease which may result in expedited diagnostics pathways. In time, AI is expected to assist in the screening of Alzheimer's through the discovery and establishment of novel biomarkers, which may in turn aid diagnosis at any earlier timepoint – at a stage where the disease exhibits the neuropathological hallmarks of the condition but without or low symptomatic presentation.

Future Alzheimer's disease therapies

There are few treatments in the market to combat these conditions at present. Existing therapies typically focus on symptom management rather than prevention, and late-stage diagnoses or diagnoses via exclusion are common, delaying treatment and lowering quality of life.

With a growing ageing population and the number of individuals living with Alzheimer's and dementia set to increase, it is evident that there is a clear gap in the market for therapies to address both disease progression and symptomatic relief. It is strongly anticipated that newer treatments will enter the market over the next decade, to confront this growing issue.

Current FDA-approved Alzheimer's drugs such as donepezil, rivastigmine, galantamine and memantine aim to reduce cognitive decline (these are acetylcholinesterase inhibitors, which work by preventing the breakdown of the neurotransmitter acetylcholine). However, these drugs do not address the mechanistic biology of Alzheimer's or halt disease progression.

41 H. Hampel, et. al., "Designing the next-generation clinical care pathway for Alzheimer's disease",
    Nature Aging, 2022.
42 *Dementia prevention, intervention, and care: 2020 report of the Lancet Commission*, op. cit.
43 X. Li, et. al., "Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2019",
    Frontiers in Aging Neuroscience, 2022.

Newer drugs are focusing on limiting aggregation of the amyloid-beta protein which leads to the classic signs of plaques on brain tissue, and thereby slowing disease, improving quality of life and limiting DALYs. In 2020 the FDA granted accelerated approval for the use of 'aducanumab', a monoclonal antibody targeting amyloid-beta plaques in the brain, the first disease-modifying treatment for Alzheimer's approved since 2003.[44] However, the drug has been marred by controversy, with several subsequent limitations published, including that it was unlikely to effectively slow cognitive and functional impairment. The US House of Representatives, Committees on Oversight and Reform, & Energy and Commerce ultimately ruled that "serious concerns about FDA's lapses in protocol" had been found.[45]

Despite these challenges, the pharmaceutical industry is backing drug development in this space. Less than two years later, the FDA approved lecanemab, a second monoclonal antibody treatment purported to clear the plaques causing cognitive impairment.[46] However, concerns remain given that that the drug needs to be infused through a vein by a medical professional and has been shown to have life-threatening side effects such as brain swelling and bleeds, requiring thorough, regular monitoring.[47]

The science of regenerative medicine
Ageing research is now focusing on regenerative medicine, the science of regrowing, repairing or replacing damaged or diseased cells, organs or tissue. This includes advancements in stem cells, tissue engineering and eventually organ production, alongside developments in immunosuppressants.

Studies have highlighted the value of telomeres, the DNA-protein structures which act as protective caps at the ends of chromosomes, as biomarkers of ageing. Telomeres naturally degrade and shorten with age each time a cell divides, reaching a critical stage when a cell stops dividing or dies, triggering senescence. This attrition is implicated in cellular ageing, with decreased telomere length (TL) linked to conditions such as diabetes, cardiovascular diseases, Alzheimer's disease and cancer, alongside an identified range of genetic and lifestyle factors.[50,51]

Telomerase, the enzyme which extends the telomeres of a chromosome, has been used to treat cells derived from patients with a premature vascular ageing syndrome, with notable increased proliferation and telomere length.[52] Telomerase gene therapy in mice has found the possibility of delaying physiological ageing and, prolonging lifespan by 20%, effectively increasing the number of times a cell can divide and turning back the clock on the cell's ageing process.[53]

Subsequently, studies have found potentially important mitigation of multiple ageing-related conditions. There is evidence that there could be positive impacts on insulin sensitivity, bone density to prevent osteoporosis and increased muscular coordination, without a reported increase in cancer rate.[54] While significant strides are required to convert lab-based science into a human clinical trial, the first glimpses of reducing senescence and premature ageing have been noted.

44 K. Y. Liu & R. Howard, "Can we learn lessons from the FDA's approval of aducanumab?", Nature Reviews Neurology, 2021.
45 The High Price of Aduhelm's Approval: An Investigation into FDA's Atypical Review Process and Biogen's Aggressive Launch Plans, U.S. House of Representatives, democrats-energycommerce.house.gov, December 2022.
46 S. Reardon, "FDA approves Alzheimer's drug lecanemab amid safety concerns", nature.com, 2023.
47 A. Abbott, "Conquering Alzheimer's: a look at the therapies of the future", nature.com, 2023.
48 S. Rizvi, et. al., "Telomere length variations in aging and age-related diseases", Current Aging Science, 2014.
49 F. Rossiello, et. al., "Telomere dysfunction in ageing and age-related diseases", Nature Cell Biology, 2022.
50 D. R. Miranda, "Scientists Prolong Mouse Lifespan by Extending Telomeres", nad.com, 2022.
51 A. Mojiri, et. al., "Telomerase therapy reverses vascular senescence and extends lifespan in progeria mice", European Heart Journal, 2021.
52 B. Bernardes de Jesus, et. al., "Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer", EMBO Molecular Medicine, 2012.

Lifestyle factors

- Behavioural and lifestyle factors can contribute to premature mortality. Metabolic health (including obesity and diabetes), smoking, vaping and opioid drug use are key risk factors for CVD, cancers and others.
- **Obesity** prevalence is fast increasing and could affect one billion people globally by 2030. However, we see that in the US obesity is rising at a declining rate, which could generate a small positive impact on mortality trends if it continues, and policy action is arresting obesity levels in other major markets.
- **Diabetes** rates continue to increase. Innovations in drugs and surgery offer some ability to mitigate the rise, with a small expected positive impact on mortality trends on the current path.
- Gains from reductions in **smoking** are wearing off, and these now make a smaller contribution to mortality improvements relative to the past. Vaping rates are low but rising.
- **Opioid**-related mortality in the US remains significant in the general population but less so among insured individuals. Other countries appear to have far less of an issue.

Lifestyle risk factors vary from daily choices in diet and exercise. Lifestyles have evolved enormously in recent centuries as technology has changed how we travel, work, manage households and family life, and spend leisure time. For example, the energy that a person expends on average on manual tasks, heavy labour and travel has fallen significantly while the ability to consume calories has exponentially increased. This evolution has caused some lifestyle risk factors for health to decline significantly while others have risen, with some becoming increasingly prominent drivers of premature mortality.

Metabolic health
Metabolic health is defined as how effectively the body generates and processes energy. A key measure of good metabolic health is a lack of insulin resistance. Insulin resistance negatively affects most of the body's key metabolic processes and presents as obesity, hypertension, raised triglycerides and lower HDL cholesterol, pre-diabetes and diabetes. Insulin resistance is also inflammatory and is associated with poor mental health and other non-communicable diseases, yet studies show it is evident in about 88–93% of US adults today.

Research is now beginning to identify insulin resistance as a significant root cause of many of today's primary drivers of mortality:

- Cancer – a recent review found that patients with a cancer diagnosis are markedly insulin resistant, and that reduced overall survival and increased cancer recurrence, perhaps as a consequence of enhanced chemoresistance of tumour cells,[53] are associated with metabolic dysfunction[54].
- CVD – all cardiovascular risks are impacted by insulin resistance. Key mechanisms leading to hypertension, raised cholesterol markers (such as elevated low-density lipoproteins (LDL) and obesity are driven by insulin resistance.
- Neurodegenerative diseases (especially Alzheimer's disease and dementias, such as vascular dementia) have a very strong association with insulin resistance, affecting both the formation of amyloid plaques and also the metabolic pathways of neurons.

The two most visible public health expressions of metabolic ill health are the rising incidence of obesity and type 2 diabetes.

Medical approaches to metabolic health have historically been siloed, treating each expression of insulin resistance separately, due to limited insight about the root cause and a lack of standardised testing for it. However, newer medicine is exploring the use of

[53] W. Li, et. al., "Effects of hyperglycemia on the progression of tumor diseases | Journal of Experimental & Clinical Cancer Research", Journal of Experimental & Clinical Cancer Research, 2019.
[54] J. M. Marmol, et. al., "Insulin resistance in patients with cancer: a systematic review and meta-analysis", Acta Oncologica, 2023.

raised fasting insulin as an early warning indicator of insulin resistance, as it can appear years or even decades before a diagnosis of poor metabolic health.

The growing use of real-time continuous glucose monitors (CGMs) may enable better prevention or management of insulin resistance.[55][56] In many countries CGMs are now available commercially for the general population, such as in smartwatches.[57] Widespread individual monitoring of blood glucose could be a driver for better metabolic health that positively impacts disease profiles and mortality.

Obesity and type 2 diabetes

Obesity, defined as having a BMI ≥30kg/m^2, is a chronic, often progressive expression of metabolic ill health and insulin resistance that leads to higher relative mortality risk. It is associated with several leading causes of preventable and premature death, including heart disease, stroke, type 2 diabetes and some cancers, with a reduction in life expectancy of 5–20 years dependent upon duration, magnitude of excess weight and other comorbidities (see Figure 11).[58]

Obesity rates have continued to steadily increase, year on year, for almost 50 years, with global rate estimated to be around 13%.[59] The US is one of the most-affected countries, with almost ~70% of adults classed as obese or overweight in both the general and insured populations, compared with ~12% in 1975.[60]

[55] J. Araujo, et. al., "Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009–2016 | Metabolic Syndrome and Related Disorders", Metabolic Syndrome and Related Disorders, 2019.
[56] M. O' Hearn et. al., "Trends and Disparities in Cardiometabolic Health Among U.S. Adults, 1999–2018", Journal of the American College of Cardiology, 2022.
[57] M. Gurman, "Apple Watch Blood Glucose Monitor Could Revolutionize Diabetes Care", bloomberg.com, 22 Feburary 2023.
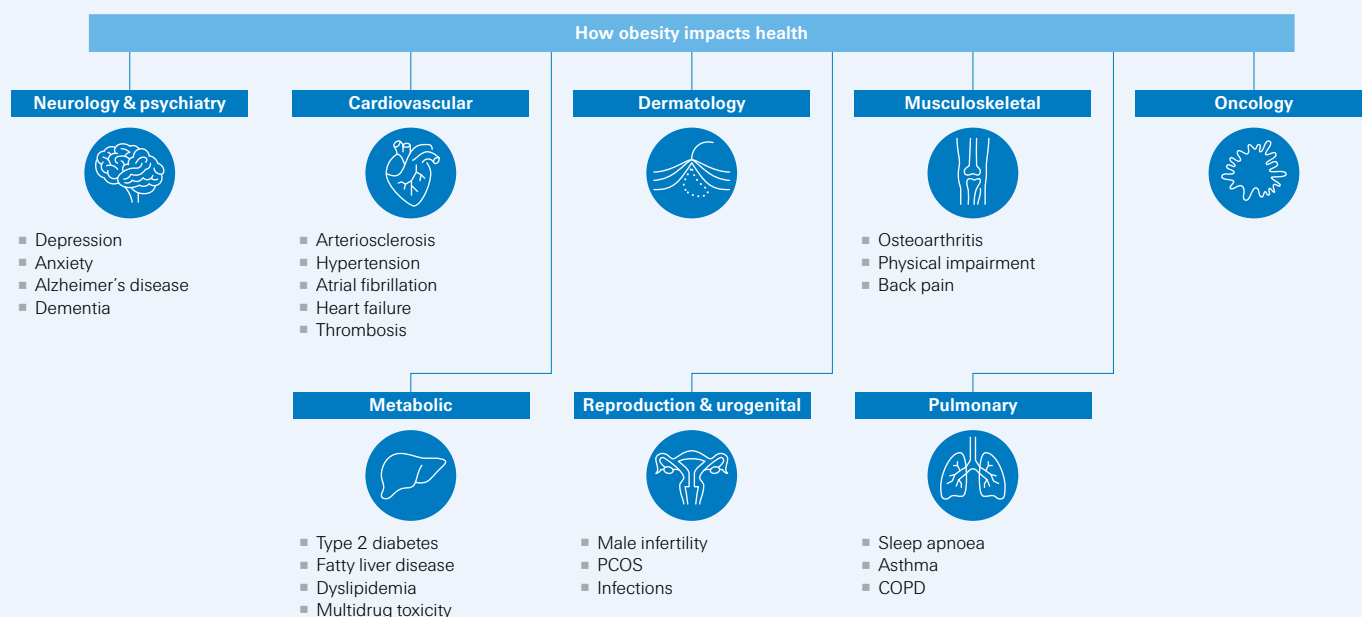[58] R. D. Muller et. al., "Anti-obesity drug discovery: advances and challenges", Nature Reviews Drug Discovery, 2022.
[59] Body mass index (BMI) , who.int, accessed May 2023.
[60] Adult Obesity Facts, cdc.gov, accessed May 2023.

Figure 11
Obesity – a multisystem health concern

How obesity impacts health

Neurology & psychiatry
- Depression
- Anxiety
- Alzheimer's disease
- Dementia

Cardiovascular
- Arteriosclerosis
- Hypertension
- Atrial fibrillation
- Heart failure
- Thrombosis

Dermatology

Musculoskeletal
- Osteoarthritis
- Physical impairment
- Back pain

Oncology

Metabolic
- Type 2 diabetes
- Fatty liver disease
- Dyslipidemia
- Multidrug toxicity

Reproduction & urogenital
- Male infertility
- PCOS
- Infections

Pulmonary
- Sleep apnoea
- Asthma
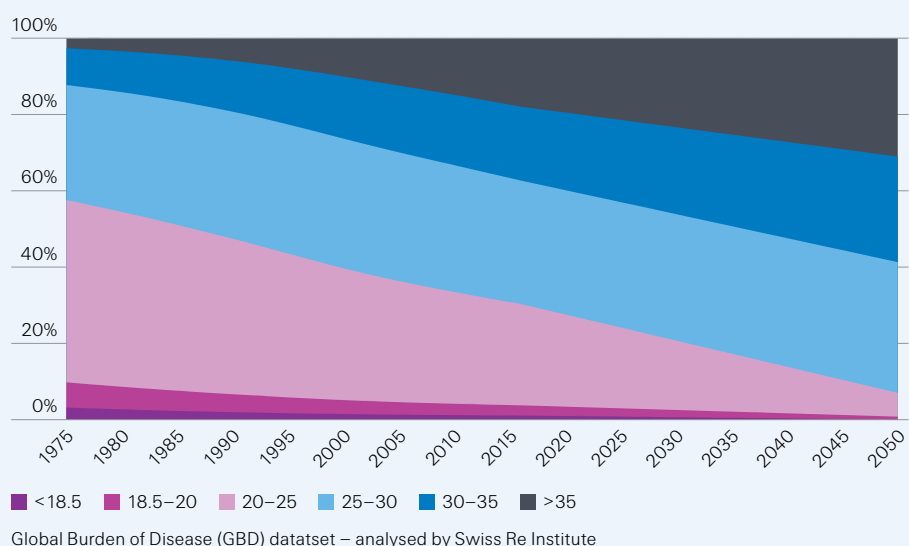- COPD

Source: Swiss Re Institute

The key driver has been the global increase in availability of ultra-processed, fast-food diets and added sugars. Countries that struggled with famine and food poverty in the 20th century now face obesity crises in the 21st. However, the shift towards automation, the rise of working from home and car travel, and increasingly urban younger populations, is also contributing to poor physical activity levels and a resultant increase in premature mortality.

Most experts expect the prevalence of obesity to go on rising, in low- and middle-income countries the fastest. The World Obesity Federation estimates that 1 in 5 women and 1 in 7 men will be living with obesity by 2030, equating to one billion people globally.[61] If the US continues on its current trajectory, it would imply that 90% of its population could be overweight or obese by 2042.

However, the pace appears to have slowed down significantly in the US since 2016. The slope of the US average age-adjusted BMI curve is starting to almost flatten. This appears to be due to positive societal shifts such as healthier eating and a departure from soft drink consumption, which may have a positive impact on mortality in the long run.

Figure 12

Historical obesity rates (proportion of population in each BMI range)

Legend: ■ <18.5 ■ 18.5−20 ■ 20−25 ■ 25−30 ■ 30−35 ■ >35

Global Burden of Disease (GBD) datatset − analysed by Swiss Re Institute

Type 2 diabetes results from chronic and frequent hyperinsulinemia (high levels of insulin in the blood), primarily due to diets high in added sugar and refined carbohydrates, which over time leads to insulin resistance, requiring the body to produce even higher levels of insulin.

About 95% of type 2 diabetes is linked to behavioural choices (diet-related and physical activity) and therefore preventable. Obesity contributes 80−85% of the risk of developing type 2 diabetes, with obese individuals seven times more likely to develop the disease.[62,63] Diabetes increases the risk of developing CVD and many other adverse outcomes including mortality, alongside organ complications such as chronic kidney disease, and elevated cancer risks.

Rates of diabetes are increasing globally. The UK and the US are on upward trajectories: the CDC projects a 3% increase in type 1 and 70% rise in type 2 diabetes in the US by 2060, if the rate of diabetes diagnoses in young people remain the same.[64]

[61] World Obesity Atlas 2022, worldobesity.org, accessed May 2023.
[62] Diabetes and Obesity, diabetes.co.uk, 2022.
[63] Adult obesity and type 2 diabetes, Public Health England, 2014.
[64] Future Surge in Diabetes Could Dramatically Impact People Under 20 in U.S., cdc.gov, 2022.

Diabetes and obesity drug development and surgical solutions
Innovations in drug development and gastric surgery suggest the future trajectories for obesity- and diabetes-related mortality may be less aggressive than the growing rates of these two conditions. The first line of treatment for type 2 diabetes is metformin, a key drug approved by the FDA in 1995 to address insulin resistance and adult-onset hypergylcaemia. Today metformin is the most prescribed glucose-lowering medication worldwide.

Long-term diabetes treatment strategies are based on lifestyle alterations such as increasing exercise, diet modifications (eg, elimination of sugar/refined carbohydrate; carbohydrate restriction to reduce insulin resistance), and occasionally bariatric surgical solutions.[65] While type 2 diabetes was previously considered chronic and progressive, today 30–50% of patients who change their diet are achieving degrees of disease remission.[66,67]

Diabetic drugs are a potential next frontier in tackling obesity because they also enable weight loss. Obesity drug therapy has historically been based on either non-specific appetite suppression, glucose breakdown and absorption regulators, or lipid and nutrient absorption inhibitors. However, limited success and significant side effects prevent their widespread use.

With increased understanding of molecular gut–brain communication and energy homeostasis, a new generation of drugs originally designed to improve insulin sensitivity in type 2 diabetic patients is being developed to treat chronic weight management. Recent FDA-approved diabetes drugs (GLP-1 receptor agonists such as liraglutide, dulaglutide, semaglutide and tirzepatide) slow gastric emptying and target certain brain receptors involved in appetite reduction, which together control food uptake, satiety and weight regulation.[68] In the short term, GLP-1 receptor agonists were found to significantly lower all-cause mortality, cardiovascular mortality and myocardial infarction, compared to comparators.[69] Treatments are increasingly being administered via weekly subcutaneous injectables rather than traditional daily drug doses, which improves treatment compliance. However, relapse and weight loss reversal are significant risks when medication is terminated. Some drug regulation bodies recommend medication for finite periods only, to support lifestyle changes.[70]

Bariatric surgeries, such as gastric bypass or sleeve gastrectomy, are now widely seen as the most effective way to treat obesity, with 90% of patients able to maintain long-term weight loss.[71] On average, 75–90% of patients that underwent bariatric surgery lost 50–70% of their excess body weight within 18 months.[72] There is increasing evidence that bariatric surgery can be a treatment option for diabetes, if hyperglycaemia is inadequately controlled by lifestyle and medical treatment. Remission of diabetes has been reported in a substantial proportion of patients.

Surgery is associated with longer life expectancy than other obesity care (~3 years) and with a lower risk of death from both CVD and cancer (~ 30% and 23% of risk reduction respectively), as per a Swedish study.[73] A larger-scale Canadian study found a 47% decrease in all-cause mortality, a 68% decrease in cardiovascular mortality and a 34% decrease in composite cardiac events for patients with type 2 diabetes and severe obesity.[74]

However, surgery is typically reserved for those with high risk of mortality and failed lifestyle interventions. Surgery also comes with peri-procedural risks (perioperative mortality ranges from 0.03% to 0.2%) and a risk of re-operation (depending on the procedure, ranges from 5% to 22%).

[65] C. J. Bailey, "Metformin: historical overview", Diabetologia, 2017.
[66] S. J. Athinarayanan et. al., "Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial", Frontiers in Endocrinology, 2019.
[67] D. Unwin et. al., "What predicts drug-free type 2 diabetes remission? Insights from an 8-year general practice service evaluation of a lower carbohydrate diet with weight loss", BMJ Nutrition, Prevention & Health, 2023.
[68] C. Anekwe, "A new treatment for obesity", health.harvard.edu, 2021.
[69] M. Monami et. al., "Effects of glucagon-like peptide-1 receptor agonists on mortality and cardiovascular events: A comprehensive meta-analysis of randomized controlled trials", Internal Journal of Cardiology, 2017.
[70] NICE recommends new drug for people living with obesity | News and features | News | NICE
[71] Bariatric Surgery for Weight Loss > Fact Sheets > Yale Medicine
[72] Duodenal Switch Provides Superior Weight Loss in the Super-O... : Annals of Surgery (lww.com)
[73] Life Expectancy after Bariatric Surgery in the Swedish Obese Subjects Study | NEJM
[74] A. G. Doumouras et. al. "Association Between Bariatric Surgery and Major Adverse Diabetes Outcomes in Patients With Diabetes and Obesity", JAMA Network Open, 2021.

Smoking and vaping

Smoking cessation is among the biggest contributors to improved health and mortality outcomes globally over the last three decades. In the US, for example, mortality among male and female smokers is approximately 200% that of non-smokers; the major causes of death in this category are cancer, respiratory and vascular diseases.[75]

Globally, adult smoking prevalence declined by 27.2% for men, and by 37.9% for women, between 1990 and 2020, with advanced markets typically seeing the largest declines. Some high-income countries saw smoking rates fall by more than 40%, while Brazil saw rates drop by 70%. However, most low- and middle-income countries have seen limited declines, with over half of all men in large populations in Asia (China, Indonesia), and in the Pacific Islands, continuing to smoke[76].

Greater public awareness of the lasting health effects of smoking, coupled with government education and support schemes, have significantly reduced uptake of smoking and have helped smokers to quit. The success of these means that further opportunities for mortality improvements are limited. Some countries, such as New Zealand, are phasing in lifetime smoking bans by age that outlaw smoking entirely for the generation of school children today.

However, in the US, uptake of electronic cigarettes is now the most common form of tobacco consumption in the adolescent population rather than smoking. As of 2020, 19.6% had used e-cigarettes or vape with nicotine-containing products, up from 1.5% in 2011.[77] While smoking rates are expected to continue to decline, the greatest drop in smoking is expected to have already occurred. By 2030, this drop is likely to flatten out, stabilising around 10% of the US population. Meanwhile, vaping is forecast to continue to grow in population, coming into parity with smoking projection by the middle of the century. Overall, however, the non-smoking rates are expected to grow as the US population turns away from consuming nicotine in any form.

Vapes are low cost and widely accessible. As a new product, their long-term relative risks are still uncertain. However, vaping may be a gateway to cigarette smoking. In the US, although smoking rates among young people are at some of the lowest levels on record, 27.5% of those who vaped in 2018 used cigarettes a year later.

Figure 13

Split of the US population: the past and projections for smoking rates
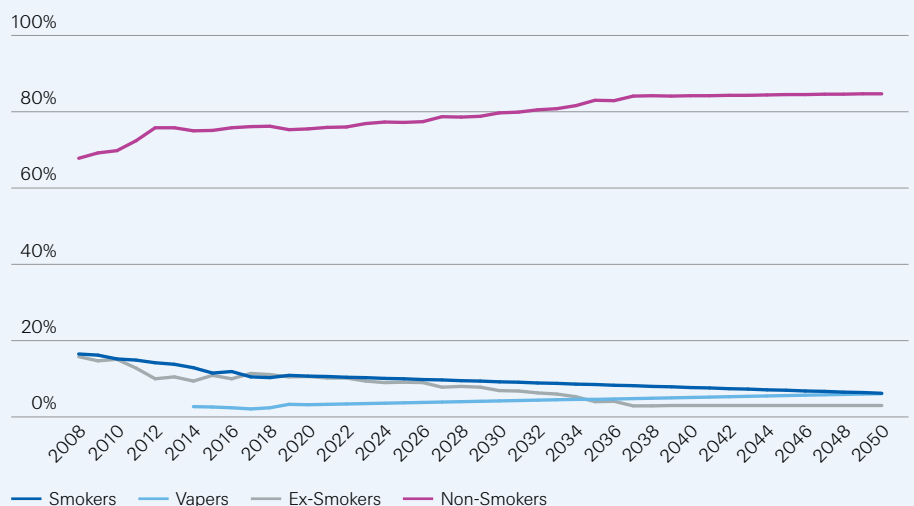
Source: OECD Health statistics 2021 – analysed by Swiss Re Institute

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[75] *Tobacco-Related Mortality*, cdc.gov, 2020.
[76] X. Dai., "Evolution of the global smoking epidemic over the past half century: strengthening the evidence base for policy action", Tobacco Control, 2022.
[77] Current Cigarette Smoking Among Adults in the United States, cdc.gov, 4 May 2023.

Opioids in the US – will the crisis abate?
The US is experiencing a severe wave of overdoses and unintentional drug poisoning deaths from opiate substances. This is widely recognised as a public health crisis with impacts on criminal justice and the economy. The wave began in 2013 and is being driven by synthetic opioids, particularly illicitly manufactured fentanyl, which continues to be found at street-level combined with heroin, counterfeit pills, and cocaine.

The annual number of deaths is rising (to a reported 28.3 deaths per 100K people in 2020)[78] but recently the rise has become more rapid, reversing all progress made on limiting deaths prior to the pandemic, and contrasting with declining deaths due to gun violence and related homicides. This is contributing to decreased US life expectancy.[79]

The US "Opioid Crisis" has existed since the 1980s,[80] and overdose deaths have increased sixfold since 1999. The current wave of opioid deaths is the third in two decades preceding 2020, after a first wave in the 1990s triggered by increased prescriptions of natural and semi-synthetic opioids and methadone, and a second wave from 2010 that saw a sharp rise in overdose deaths driven by heroin use. Insured populations are reported to have been affected far less by the crisis.

Stricter laws around prescribing such drugs, and more grassroots action to address this problem, give hope that the crisis may abate in time.

Figure 14
Opioid -related deaths in the US population, by type (death rate per 100K)
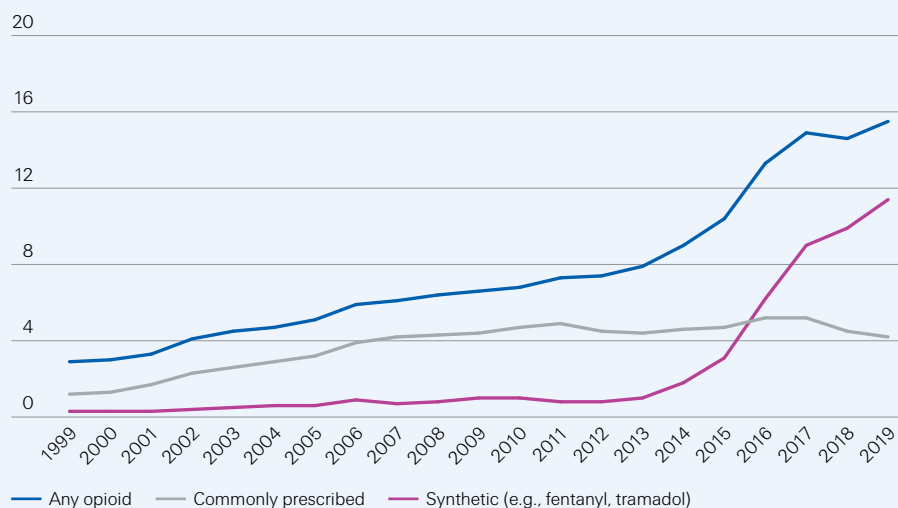
Source: US CDC – analysed by Swiss Re Institute

Legend: Any opioid — Commonly prescribed — Synthetic (e.g., fentanyl, tramadol)

[78] *Death Rate Maps & Graphs,* cdc.gov, 2022.
[79] C. Klobucista., et.al, "Fentanyl and the U.S. Opioid Epidemic", Council on Foreign Relations, 19 April 2023.
[80] S. Harper., et. al.," Declining Life Expectancy in the United States: Missing the Trees for the Forest", Annual Review of Public Health, 2021.

Emerging topics

Mortality improvement over the long term can be influenced by many factors not captured in either past experience data or the likely medical advancements we are aware of today. We monitor emerging trends that may offer opportunities for stronger mortality improvement in decades to come, and as yet unquantifiable risks that could have a negative impact.

Artificial intelligence (AI)

Artificial intelligence is already in use today to support cancer diagnostics. AI and machine learning algorithms analyse imaging and screening data from mammograms, CT and MRI scans, as well as pathology images from tissue biopsies. AI also now features in drug discovery, to identify and accelerate the process of identifying new targets[81]. We expect these technologies to enhance medical advancements, "nudge" lifestyle factors via wearable devices, and improve medical decision making and diagnoses of many conditions.

The recent explosion of ChatGPT and other large language models offers the potential to revolutionise medical innovation and research.[82] Advanced natural language processing capabilities can aid clinical decision-making and medical research. The integration of such technology into medical software may provide rapid information and allow professionals to develop prompt, personalised treatment plans based on symptoms, medical history and other factors (see Figure 15).

This technology may also assist in clinical research by synthesising and analysing large datasets, identifying patterns and trends, and predicting outcomes, thereby providing insights into potential diagnoses, treatment options, and prognosis. The ability to rapidly

81 N. Savage, "Tapping into the drug discovery potential of AI" Nature News Feature, 2021.
82 Will ChatGPT transform healthcare?, Nature Medicine, 2023.

Figure 15
Integrated data – the future of electronic healthcare records

Source: Swiss Re Institute

analyse vast amounts of medical literature could accelerate drug discovery and development by identifying potential drug targets.

Climate change

Climate change is expected to affect human health primarily through extreme heat, air pollution, and increased exposure to infectious disease spread by non-human vectors. This is anticipated to lead to higher morbidity of non-communicable diseases, particularly CVD, respiratory illnesses, cancers, and increased spread and emergence of tropical infectious diseases. Climate change will likely pose the greatest health risk to clinically vulnerable individuals with comorbidities, and groups such as the elderly, the disabled, pregnant women and children. Frail, ageing populations could push mortality rates higher.

The extent of an individual's direct exposure to risk factors, and access to mitigation tools, is the greatest determinant of their overall risk profile. Inequality in a person's vulnerability to climate change is linked to their **exposure, sensitivity,** and **adaptive capability.** Exposure refers to the degree to which an individual is exposed to the elements, examples of which include individuals employed under climate-strenuous conditions; sensitivity refers to underlying health conditions and age, which are known to be additive and exaggerative factors; and finally adaptive capacity which is dependent upon an individual's ability to adjust to changing climates by alleviating or mitigating risk, such as purchasing cooling systems, hydration or air filtration devices, among others. All of these are heavily influenced by social factors such as wealth and access to healthcare.

The effects of climate change on health are expected to be gradual and incremental over the long term. Certain trends can be estimated with some accuracy, such as extreme heat, or the pace of technological change to mitigate climate risks. However, factors such as air pollution and infectious diseases are far more uncertain, with a wide range of plausible outcomes. Mitigation tools such as cooling, hydration and air filtration can greatly reduce health risks, but risk interdependence is a key consideration given the reliance on electricity, which could increase warming and air pollution through fossil fuel usage.

The insured population is likely to be better placed to reduce exposure to the elements and to have greater access to mitigation measures than the global population overall. While some long-term health deterioration due to extended exposure may be expected, this is likely small relative to other biological risk factors and offset by the positive impact of air quality improvement in certain regions.

Pandemics and zoonotic diseases

As seen with COVID-19, zoonotic diseases have the potential to spread globally, overwhelm global healthcare systems and significantly impact acute mortality (see Figure 16).

Zoonotic diseases arise through cross-species transmission, with the infective pathogen derived from animal-to human spillover from wildlife. Approximately 60–75% of human infectious diseases are a consequence of pathogens originating from other species. Influenza, for example, is a remnant of this process: a family of viruses that spread from animals but is now a leading cause of mortality globally. Similarly, the SARS-CoV-2 virus (COVID-19) is also likely to have spilled over from an animal reservoir and into humans and other animals.

This phenomenon is likely becoming more frequent due to factors such as habitat change including deforestation, climate change, and encroachment of humans into previously isolated animal territories. Spillovers from high-risk, isolated reservoirs (species with resilient immune systems) have resulted in greater animal-to-animal and animal-to human disease transmission, leading to epidemics such as of Ebola and Zika.

Climate change is a strong driver of zoonotic disease, with increasing global travel and mobility as triggers for a pandemic from initial local or endemic risk pools.[83] Rising global temperatures and altered precipitation and humidity patterns are increasing out-of-cycle, non-seasonal vectoral breeding and increased transmission venturing further outwards from tropical climates.

Climate change is predicted to drive 3,870 species of wild mammals into new areas by 2070, leading to an estimated more than 300000 new cross-species encounters, most likely in Africa and southeast Asia. This has the potential to generate 15,000 virus-sharing events by 2040.[84]
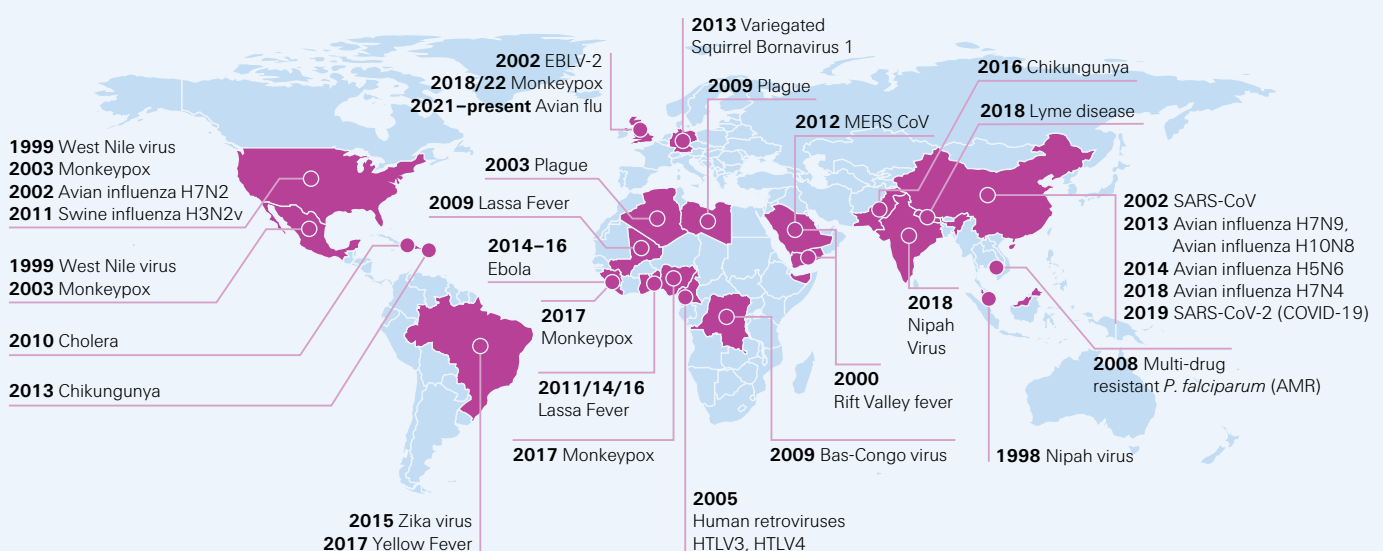
As global infection patterns evolve, previously unexposed populations may be at risk of exposure to new vector-borne diseases, unfamiliar to their inhabitants. Not every disease is likely to cause substantial threats to life, however, there is an underlying risk that a new, serious infection could pose serious health concerns.

[83] The risk of a lifetime: mapping the impact of climate change on life and health risks, Swiss Re Institute, 3 January 2023.
[84] C Carlson, et.al., "Climate change increases cross-species viral transmission risk", Nature, 2022.

Figure 16
Global significant zoonotic disease outbreaks since 1998

2013 Variegated Squirrel Bornavirus 1
2002 EBLV-2
2018/22 Monkeypox
2021−present Avian flu
2009 Plague
2016 Chikungunya
2012 MERS CoV
2018 Lyme disease

1999 West Nile virus
2003 Monkeypox
2002 Avian influenza H7N2
2011 Swine influenza H3N2v

2003 Plague
2009 Lassa Fever
2014–16 Ebola

2002 SARS-CoV
2013 Avian influenza H7N9, Avian influenza H10N8
2014 Avian influenza H5N6
2018 Avian influenza H7N4
2019 SARS-CoV-2 (COVID-19)

1999 West Nile virus
2003 Monkeypox

2010 Cholera

2013 Chikungunya

2017 Monkeypox

2011/14/16 Lassa Fever

2018 Nipah Virus

2008 Multi-drug resistant *P. falciparum* (AMR)

2000 Rift Valley fever

2009 Bas-Congo virus

1998 Nipah virus

2017 Monkeypox

2005 Human retroviruses HTLV3, HTLV4

2015 Zika virus
2017 Yellow Fever

Source: Swiss Re Institute

Antimicrobial resistance

Antimicrobial resistance (AMR) is a growing threat to global public health that is occurring as bacterial, viral, fungal, or parasitic evolution leads to resistance to drugs used to treat infections, with potentially fatal outcomes. AMR can make infections more difficult to treat, leading to increased mortality rates, with a more pronounced risk for vulnerable populations, such as children, the elderly, and people with weakened immune systems.

As an increased number of pathogens exhibit resistance to existing antimicrobials, further treatment options become limited, increasing healthcare costs for the individual and progressively worsening health outcomes. There is the additional risk of reduced effectiveness of health interventions including procedures which rely on antimicrobial drug efficacy such as chemotherapy, organ transplants and other surgeries.

To address the threat of AMR, it is crucial to reduce the misuse and overuse of antimicrobials, implement effective infection prevention and control measures, and continue to develop new pharmaceutical treatments. AMR is becoming an increasing problem which can complicate and interfere with current treatment regimes and may result in sepsis, organ failure and increased mortality.

Sepsis is a life-threatening dysregulated immune system response to an infection that causes tissue damage and multiple organ failure. The WHO describes sepsis as "a frequently final common pathway to death from many infectious diseases". In 2017 sepsis was responsible for 20% of global deaths, 10% of which occurred in children.[85] Sepsis accounts for 20% of US hospital admissions and more than 50% of US hospital deaths.[86] Infections that progress to sepsis can be acquired in both community and hospital settings; the outcomes of the latter are significantly more adverse with 40% mortality in ICUs worldwide.[87] The incidence of sepsis also sharply increases with age, particularly in people over the age of 80, and is associated with very high mortality rates.[88]

Sepsis treatment is highly time sensitive so earlier detection and better management is crucial to prevent mortality. Healthcare setting-acquired infections may be antibiotic-resistant and can rapidly deteriorate clinical conditions.

Autonomous driving

Globally, road traffic-related deaths averaged 17.4 per 100 000 population as of 2015, according to the WHO, with significant disparities between regions, gender and age. As countries move towards cleaner, green energy, demand for electric autonomous vehicles (AV) is rising and AV car sales are projected to represent 25% of the global market by 2035.[89]

Since 94% of traffic fatalities are caused by human error, autonomous 'self-driving' or 'driverless' vehicles are predicted to meaningfully reduce driving accident mortality by up to 90%. it is estimated that globally, AVs could save 10 million lives per decade through a combination of collision prevention and minimisation of post-crash injury.[90] However, this will likely take several years as autonomous vehicles gain traction, and hence could lead to long term mortality improvements.

85 *Sepsis*, World Health Organisation, 26 August 2020.
86 I. Klaz, "Balancing sepsis care and antimicrobial stewardship", Wolters-Kluwer, 15 March 2022.
87 R. Makwat, et. al., "Epidemiology and burden of sepsis acquired in hospitals and intensive care units: a systematic review and meta-analysis", Intensive Care Medicine, 2020.
88 I. Martin-Loeches, et. al., " Risk factors for mortality in elderly and very elderly critically ill patients with sepsis: a prospective, observational, multicenter cohort study", Annals of Intensive Care, 2019.
89 *The Most Revolutionary Thing About Self-Driving Cars Isn't What You Think*, Forbes, 20 June 2017.
90 J. Fleetwood, "Public Health, Ethics, and Autonomous Vehicles", American Journal of Public Health, 2017.

Conclusion

Medical innovation and progress are expanding our ability to live longer, healthier lives. The improvement in the past century has been dramatic as vast developments in basic healthcare, nutrition, and the increasingly widespread use of antimicrobial drugs to treat infectious diseases brought huge declines in premature mortality. Attention has since shifted to longevity, to find the upper limits of healthy life expectancy. We are optimistic of seeing sustained life expectancy gains over the long term.

Perhaps the biggest wave of mortality improvement in the second half of the 20th century was driven by lifestyle change in the form of smoking cessation, reinforced by the pharmaceutical development of CVD drugs. These strongly improved heart attack and stroke-driven premature mortality in most age groups and led to reductions in many other major causes of death. We still benefit today from lower smoking rates, greater medical and lifestyle awareness, and public policy interventions.

We see the transformation of cancer treatment as a likely key driver of the next wave of improvements, as therapies increasingly become more personalised and targeted, with a growing role for AI in early detection and screening. We anticipate fewer mortality improvements than in the past from CVD, with future change primarily driven by individual behaviours and interventions targeting underlying risk factors such as diet and exercise – and ensuring better compliance with medical advisory and preventive treatment options.

The prevalence of neurodegenerative and ageing diseases is expected to rise in the coming decades given population ageing, yet therapies to address these diseases are in their infancy. We expect considerable gains in longevity as the science of diagnostics and treatments for these conditions moves forward.

New risk factors for premature mortality are continually emerging that could reduce future improvements. One major risk is from lifestyle factors, principally driven by poorer diets and declining physical activity. Countries that struggled with famine and food poverty in the 20th century now face obesity crises in the 21st. These lifestyle risks are, however, controllable through societal and individual actions. Through a combination of public health policy actions in raising awareness, medical guidelines taking a more aggressive stance in fighting this epidemic, and a range of available and future technologies and treatments (wearables, obesity drugs, etc.), we are optimistic that solutions may be found that will alleviate the disease burden over the very long timeframes considered here. Other developments that represent potential headwinds are antimicrobial resistance, climate change and novel infectious diseases.

On balance we see a strong case for continued mortality improvements over the long term, even as the uncertainty on timing remains high. This is a testimony to the unparalleled levels of investment and resources that have and continue to be invested by society in finding cure for diseases, public health policies geared towards improving health and longevity for vast swathes of society, and individuals taking responsibility towards their own health.

The editorial deadline for this study was 18 May 2023.