

CELEBRATING INNOVATION





The outlook on health care in Mexico was very different in 1950, when the Association of Producers and Importers of Medicinal Goods –which changed its name to Mexican Association of Pharmaceutical Research Industries (AMIIF) in 1994– was founded. Life expectancy then was around 48 years. Infectious diseases, such as pneumonia, gastroenteritis, typhus, and measles, caused 56% of deaths, accounting for 78% of deaths in children.

However, on that year a major change, driven by two pharmaceutical innovations, was already underway. The development of vaccines was one of these innovations that began eliminating or eradicating diseases such as whooping cough, measles, and smallpox, which were still the cause of 6% of deaths in children in 1950.

Antibiotics were the second innovation that put an end to an era in which there were no tools to treat infections lurking in the air and water. The outcome of these often-deadly diseases depended solely on a healthy immune system. In 1940, 1.1% of all deaths in Mexico were caused by bacterial infections that could be controlled with penicillin, specifically syphilis, and diphtheria. By 1950, this number was down to 0.6%, falling further to 0.3% by 1960.

In the following seven decades, the effects of these innovations, together with the expansion of hospital and health care services, allowed for a dramatic increase in average life expectancy in Mexico, which is now 75 years—an additional 28 years compared to 1950. Vaccines and antibiotics alone are estimated to be responsible for a 20-year increase in life expectancy worldwide.

The world we know would not exist without the pharmaceutical advances of the last decades. The world of tomorrow will also depend on the progress we make today.



Control of infectious diseases, the growing number of people at advanced ages, and the increase in risk factors such as obesity and a sedentary lifestyle produced an epidemiological transition in Mexico that became fully evident in the 1980s, when chronic noncommunicable diseases appeared on the stage to become the nation's leading cause of death.

Cardiovascular diseases, cancer, and diabetes are the most pressing issues in health care today, as they account for millions of deaths worldwide, reduce the quality of life of millions more, and place a heavy economic burden on people and health care systems alike.

For 70 years, pharmaceutical innovation has stepped up to the plate to address these challenging issues and produced favorable results. Diabetes stopped being a deadly illness and became a manageable disease with a close-to-average life expectancy. Improved therapeutic alternatives have successfully reduced cardiovascular diseases between 61% and 74% in many countries worldwide. Cancer death rates have fallen 23% from their peak in 1991.

Pharmaceutical innovation has met both these long-term and emerging challenges.

In 1981, HIV/AIDS, a hitherto unknown disease, became an epidemic. In the early years, most AIDS patients died within a year after the disease was diagnosed. With early detection and adherence to treatment, people with HIV can live a normal lifespan.

And just 2 years ago, COVID-19, another hitherto unknown disease, unleashed a health crisis without recent precedents, whose consequences have touched all areas of human life and rapidly disrupted the global landscape with force. The history of this crisis is still being written.



This book takes a look at six essential areas in the history of pharmaceutical innovation over the past 70 years: vaccines, antibiotics, cardiovascular diseases, diabetes, cancer, and HIV/AIDS. It is not a complete story but aims to provide an overview of how innovation works by pointing to key moments and critical discoveries.

Innovation means creating new and better things. In the pharmaceutical industry, innovation is the quest for increasingly effective therapeutic options to prevent and treat diseases—the pursuit of solutions that minimize risk for the people who use them with simplified medical management. First and foremost, it is a story about progress.

Innovation is both a process and an outcome. It is a process that involves hundreds of thousands of people working at different times and in different places—sometimes simultaneously—whose work is connected in ways that are not always obvious. At the end and the beginning of this process are the people whose needs give a sense to innovation and benefit from its fruits: those who suffer from a disease, those who are at risk of becoming sick, and those who have never been ill, but could get sick. People's well-being and quality of life serve as the

Main Death Causes in Mexico, 1922-2020

■ Noncommunicable diseases
 ■ Communicable diseases
 ■ Other causes

| | 1st | 2nd | 3rd | 4th | 5th | 6th | 7th | 8th | 9th | 10th |
|------|-------------------------------------|---|---|--|---|---|--|--|---|--|
| 1922 | Pneumonia/ Influenza | Diarrheas/ Enteritis | Malarial fever and cahexia | Whooping cough | Smallpox | Congenital debility | Pulmonary tuberculosis | Violent deaths | Bronchitis | Senility |
| 1930 | Diarrheas/ Enteritis | Pneumonia/ Influenza | Malarial fever and cahexia | Whooping cough | Smallpox | Measles | Congenital debility | Congenital debility | Violent deaths | Bronchitis |
| 1940 | Diarrheas/ Enteritis | Flu and pneumonia | Malaria | Violent or accidental deaths | Measles | Bronchitis | Liver disease | Liver disease | Pulmonary tuberculosis | Dysentery |
| 1950 | Gastro- enteritis and colitis | Flu and pneumonia | Certain early childhood illnesses | Accidents, poisonings and violence | Malaria | Whooping cough | Cirrhosis of the liver | Pulmonary tuberculosis | Bronchitis | Measles |
| 1960 | Gastro- enteritis and colitis | Flu and pneumonia | Certain early childhood illnesses | Accidents | Malignant tumors | Homicides | Bronchitis | Pulmonary tuberculosis | Cirrhosis of the liver | Malaria |
| 1970 | Pneumonia / Influenza | Enteritis and other diarrheal diseases | Cardio- vascular diseases | Certain early childhood illnesses | Malignant tumors | Cerebro- vascular diseases | Measles | Accidents | Cirrhosis of the liver | Acute respiratory infection |
| 1980 | Accidents | Gastro- intestinal diseases | Pneumonia/ Influenza | Cardio- vascular diseases | Malignant tumors | Certain early childhood illnesses | Cerebro- vascular diseases | Cirrhosis and other liver diseases | Diabetes mellitus | Homicide and injuries |
| 1990 | Cardio- vascular diseases | Malignant tumors | Accidents | Diabetes mellitus | Certain conditions originating in the perinatal period | Pneumonia/ Influenza | Gastro- intestinal diseases | Cerebro- vascular diseases | Cirrhosis and other liver diseases | Homicide and injuries |
| 2000 | Diabetes mellitus | Cardio- vascular diseases | Cirrhosis and other liver diseases | Cerebro- vascular diseases | Certain conditions originating in the perinatal period | Enfermedad pulmonar obstructiva crónica | Chronic obstructive pulmonary disease | Vehicle collisions | Homicide and aggressions | Nephritis and nephrosis |
| 2005 | Diabetes mellitus | Cardio- vascular diseases | Cirrhosis and other liver diseases | Cerebro- vascular diseases | Chronic obstructive pulmonary disease | Certain conditions originating in the perinatal period | Vehicle collisions | Chronic obstructive pulmonary disease | Hipertensive heart disease | Nephritis and nephrosis |
| 2017 | Cardio- vascular diseases | Diabetes mellitus | Malignant tumors | Liver diseases | Accidents | Cerebro- vascular diseases | Aggressions (homicides) | Chronic obstructive pulmonary disease | Pneumonia/ Influenza | Renal insufficiency |
| 2020 | Cardio- vascular diseases | Covid-19 | Diabetes mellitus | Malignant tumors | Pneumonia/ Influenza | Liver diseases | Cerebro- vascular diseases | Aggressions (homicides) | Accidents | Chronic obstructive pulmonary disease |

beacon guiding the path to pharmaceutical innovation.

In retrospect, it is easy to perceive this as a path without deviations, where each step is the inevitable consequence of the previous one, with each new class of medications predestined to exist. However, this is not the case, as innovation takes a winding path between stumbles and serendipitous encounters.

There are multiple examples to illustrate this fact. There was a 32-year span between the discovery of a substance called guanidine, a blood glucose-lowering agent in animals, and research that confirmed that the guanidine derivative metformin was an effective hypoglycemic drug. Guanidines were practically forgotten along the way. Zidovudine, which became available in 1986 as the first antiviral treatment for HIV, was originally developed in the 1960s to thwart cancer, but it did not work. The origins of the first effective chemotherapy for cancer were based on findings linked to chemical weapons used on the battlefields during World War I.

If these innovations have derived or are to derive benefits for people, it is because of the incremental innovation process that per-

mits a discovery whose feasibility was not apparent at first to be taken up at a later date, with the tools and knowledge required to understand their usefulness and unleash their capabilities.

Many medications are a regular part of our daily routine. They are so ubiquitous

that it is easy to forget that they were originally innovative. In 1987, when the FDA cleared the first statins, it was difficult to anticipate that they would become one of the most widely used classes of medications in the world over time.

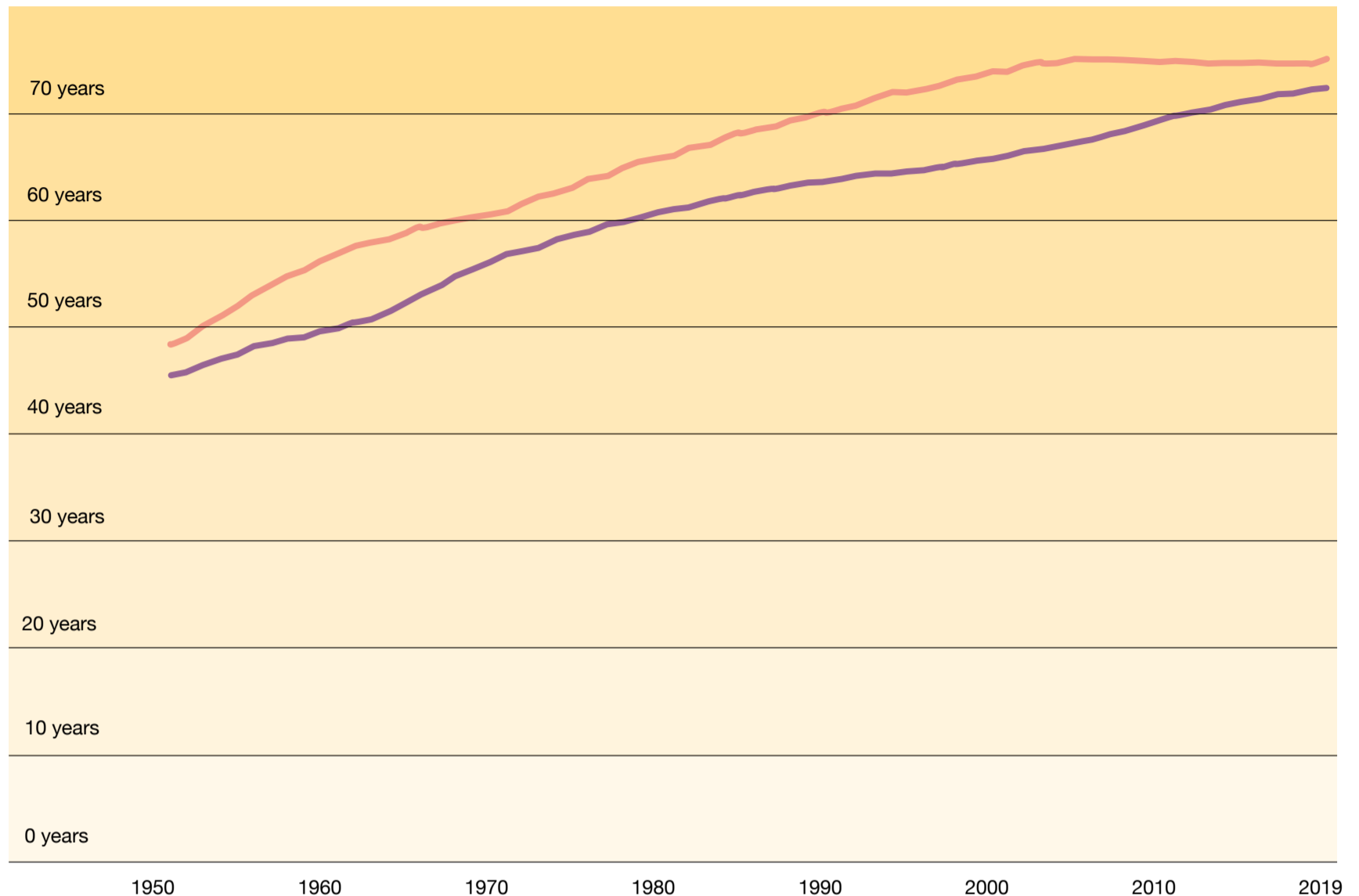
The actual potential of a new medication is unknown at first. However, it can also continue to grow over time

as that molecule is studied. Aspirin went on the market in 1899 to alleviate pain. Its effectiveness as an antiplatelet agent was confirmed in 1974, and it is still widely used for that purpose. Today's innovative treatments, such as immunotherapies and monoclonal antibodies, with their incomplete stories, could follow similar paths and become part of the future of our daily landscape.



70 years have gone by since the Association of Producers and Importers of Medicinal Goods – now AMIIF – was founded.

Life expectancy, 1950-2019



Source: Our World in Data.

There are no final results when it comes to innovation.

Innovation does not depend on the stroke of genius or a moment of inspiration. It is a well-known fact that Alexander Fleming discovered penicillin. It is less well known that this finding would not have had the same impact without the follow-up done by Florey and Chain, who kept up the research until

they developed a method to purify penicillin in large amounts, laying the ground for the first clinical trials and industrial production. The discovery or identification of a substance is only the first step in a long process that is not free from risks. On average, it takes 10 to 15 years from the time new medicine research begins to reach the marketplace. The cost of developing each new medication involves billions of dollars. Only 5 in 5,000 molecules researched evolve to human testing, and only one actually makes it to the market as a new drug. The history of innovation tends to record successful advances, but setbacks, which are much more commonplace, are also part of the story.

Medications and medical advances cannot be taken for granted. Despite high coverage rates, vaccination achievements are challenged by the progress made by anti-vaccine groups. Antimicrobial resistance threatens to erase much of the gains made with antibiotics. The relaxation of daily measures to stop its transmission—an unexpected consequence of the successful fight against HIV/AIDS—could undermine efforts to contain the epidemic. Without adequate prevention efforts, cardiovascular diseases and diabetes will continue to burden health

care systems. Cancer is still an open chapter in medicine, and its cure is one of the most cherished and elusive wishes.



In that sense, the history of innovation is unfinished. Addressing these and other health problems requires continuing efforts to research and produce new therapeutic alternatives and make them available to those who need them. The COVID-19 pandemic has been a litmus test for the biopharmaceutical industry, which has worked at an unprecedented speed to research and develop hundreds of potential weapons against the pandemic and to meet the vast demand for vaccines. It has also tested health care authorities worldwide, who have had to expand their hospital care capacities and launch vaccination campaigns at an unprecedented scale. The successful cooperation ecosystem launched in this health crisis reminds us that the public sector, academia, the private sector, civil society organizations, and international organizations must work together to face the biggest health challenges of the 21st century. We have said it before and repeat it today: we are all co-responsible when it comes to health.

Awareness of the challenges we face should not cause us to neglect progress. The world we know—and I repeat—would not exist without it. The world of tomorrow will also depend on the progress we make today. We wrote this book to celebrate the past, present, and future of innovation.



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