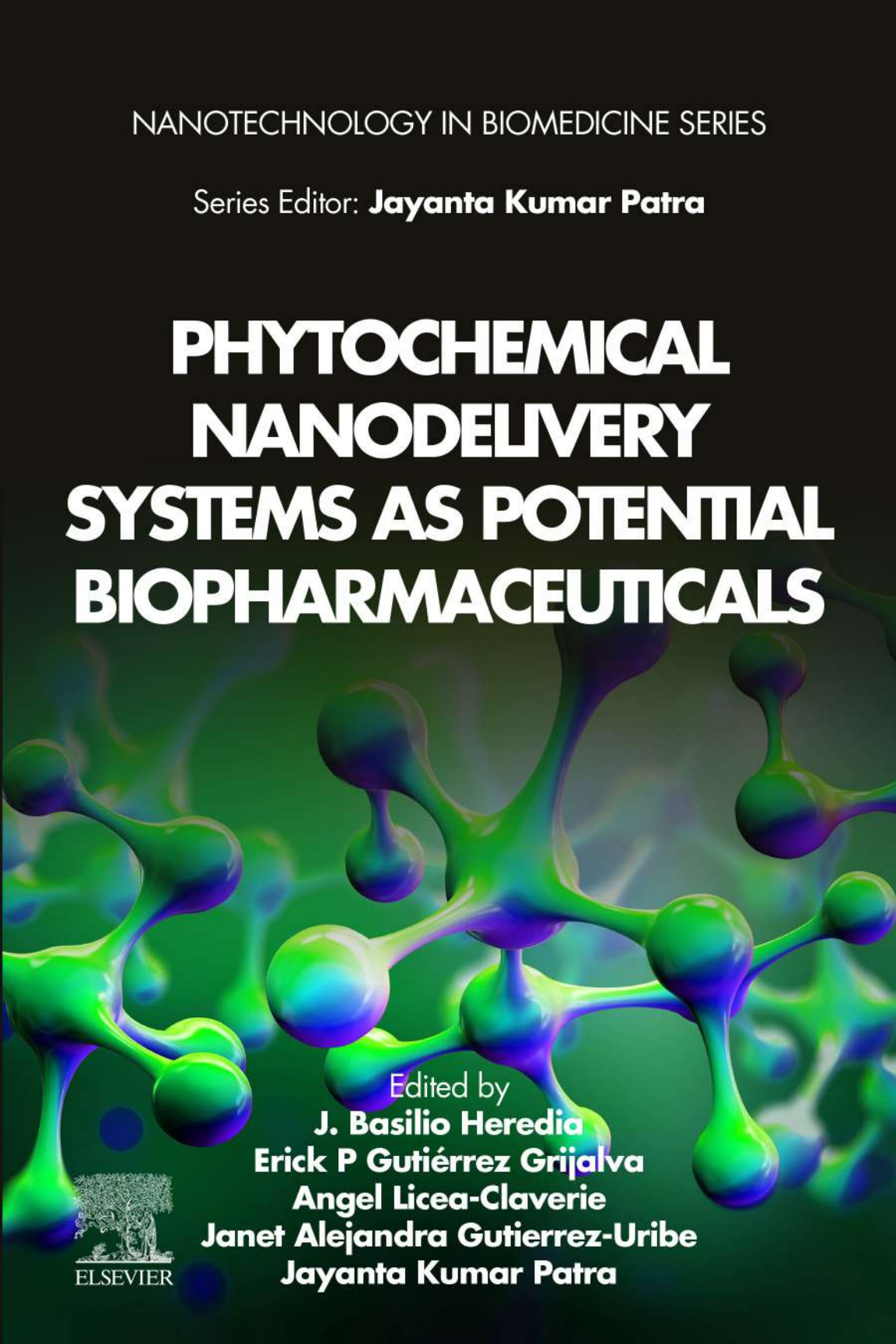
NANOTECHNOLOGY IN BIOMEDICINE SERIES

Series Editor: **Jayanta Kumar Patra**

PHYTOCHEMICAL NANODELIVERY SYSTEMS AS POTENTIAL BIOPHARMACEUTICALS



Edited by
J. Basilio Heredia
Erick P Gutiérrez Grijalva
Angel Licea-Claverie
Janet Alejandra Gutierrez-Uribe
Jayanta Kumar Patra

ELSEVIER

PHYTOCHEMICAL NANODELIVERY SYSTEMS AS POTENTIAL BIOPHARMACEUTICALS

Edited by **J. Basilio Heredia, Erick P. Gutiérrez-Grijalva, Angel Licea-Claverie, Janet Alejandra Gutierrez-Uribe and Jayanta Kumar Patra**

Nanotechnology in Biomedicine series

Describes nanoencapsulation technologies applied to phytochemicals using a biopharmaceutical approach

Phytochemical Nanodelivery Systems as Potential Biopharmaceuticals comprehensively reviews current information on nanotechnology applied to phytochemical nanoencapsulation to enhance the bioavailability and bioactivity.

The book is divided into two sections; the first section critically reviews current information on the field of nanotechnology and phytochemicals, and the second section highlights the preclinical and clinical studies of phytochemicals to comprehensively review the efficacy of these molecules as drugs of human use. This book provides a useful overview of this rapidly evolving field for materials scientists and pharmaceutical scientists as well as for those with interest in biopharmaceuticals from plant sources, such as organic chemists and food scientists.

Key Features

- Provides an introduction to both phytochemicals and nanomaterials for use in biopharmaceutics, allowing both materials scientists and pharmaceutical scientists to gain a basic understanding of each field
- Reviews key phytochemical types for use as biopharmaceuticals, including terpenes, alkaloids, and glucosinolates, among others
- Explores the various nanomaterials and nanoencapsulation techniques for administration of phytochemical nanoformulations

About the Editors

J. Basilio Heredia is a senior researcher at the CONACYT-Centro de Investigación en Alimentación y Desarrollo, Culiacán, México. Since 1996, he has been an active member of the Food Science and Technology Group. His research lines are functional foods and nutraceuticals, secondary plant metabolism, stress and molecular signaling, and plant biomass as a source for antioxidants and bioactive compounds.

Erick P. Gutiérrez Grijalva is a researcher at CONACYT-Centro de Investigación en Alimentación y Desarrollo, A.C. His research lines are bioaccessibility of bioactive compounds, metabolomics of Mexican plants, and extraction technologies of secondary metabolites.

Angel Licea-Claverie is a full-time professor at the Instituto Tecnológico de Tijuana, which is part of the Tecnológico Nacional de México. He has 20 years of experience in the study of temperature- and pH-sensitive polymers and 14 years of experience on controlled radical polymerization techniques. His research group have studied the controlled release of antiinflammatory and anticancer drugs from the sensitive polymeric materials developed.

Janet A. Gutierrez-Uribe is an associate research professor at Tecnológico de Monterrey, México, and a leader of the Healthy Foods Unit at The Institute for Obesity Research. She won the "Rómulo Garza 2021" award in its INSIGNIA category for her relevant career as a researcher at the Tecnológico de Monterrey. She is the winner of the 2020 Research Award for young scientists awarded by the Mexican Academy of Sciences. For more than 15 years, she has been dedicated to researching the properties of food for the treatment and prevention of chronic-degenerative diseases.

Jayanta Kumar Patra is an associate professor at Dongguk University, Republic of Korea. He has around 14 years of research and teaching experience in the fields of pharmacology and nanobiotechnology. His current research focuses on nanoparticle synthesis by green technology methods and associated biomedical applications: green synthesis of silver, gold, iron, calcium, and phosphorous nanoparticles using food waste, agricultural waste, and plant materials and evaluation of their antibacterial, antioxidant, and cytotoxicity potential.

ISBN 978-0-323-90390-5

9 780323 903905

ELSEVIER elsevier.com/books-and-journals

Nanotechnology in Biomedicine

PHYTOCHEMICAL NANODELIVERY SYSTEMS AS POTENTIAL BIOPHARMACEUTICALS

Edited by

J. BASILIO HEREDIA
Research Professor, Research Center for Food and Development, Culiacan, Sinaloa, Mexico

ERICK P. GUTIÉRREZ-GRIJALVA
Cátedras CONACYT—Research Center for Food and Development, AC, Culiacán, Sinaloa, Mexico

ANGEL LICEA-CLAVERIE
Full-time Professor, Centro de Graduados e Investigación en Química, Tecnológico Nacional de México/Instituto Tecnológico de Tijuana, Tijuana, Baja California, Mexico

JANET ALEJANDRA GUTIERREZ-URIBE
Associate Professor, Tecnologico de Monterrey, School of Engineering and Sciences, Monterrey, Mexico
Healthy Foods Unit Leader, The Institute for Obesity Research, Tecnologico de Monterrey, Monterrey, Mexico

JAYANTA KUMAR PATRA
Associate Professor, Research Institute of Integrative Life Sciences, Dongguk University, Goyangsi, Republic of Korea

Series Editor

JAYANTA KUMAR PATRA

ELSEVIER

Elsevier
Radarweg 29, PO Box 211, 1000 AE Amsterdam, Netherlands
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States

Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

ISBN: 978-0-323-90390-5

Publisher: Matthew Deans
Acquisitions Editor: Sabrina Webber
Editorial Project Manager: Clodagh Holland-Borosh
Production Project Manager: Nirmala Arumugam
Cover Designer: Greg Harris

Typeset by STRAIVE, India

Contents

Contributors

Dulce Libna Ambriz-Pérez
Polytechnic University of Sinaloa, Mazatlán, Sinaloa, Mexico

Marilena Antunes-Ricardo
Tecnologico de Monterrey, School of Engineering and Science; Tecnologico de Monterrey, The Institute for Obesity Research, Monterrey, NL, Mexico

Sara Aviles-Gaxiola
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Jorge Benavides
Tecnologico de Monterrey, The Institute for Obesity Research; Tecnologico de Monterrey, Escuela de Ingeniería y Ciencias, Monterrey, NL, Mexico

Magdalena Elizabeth Bergés-Tiznado
Academic Unit of Engineering in Environmental Technology, Polytechnic University of Sinaloa, Mazatlán, Sinaloa, Mexico

Luis Angel Cabanillas-Bojórquez
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Yadira Denisse Cerda-Sumbarda
Centro de Graduados e Investigación en Química, Tecnológico Nacional de México/ Instituto Tecnológico de Tijuana, Tijuana, Baja California, Mexico

Laura Aracely Contreras-Angulo
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Marilyn S. Criollo-Mendoza
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Cristina A. Elizalde-Romero
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Israel García-Aguiar
Universidad Autónoma de Occidente, Unidad Regional Culiacán, Boulevard Lola Beltrán, Culiacán, Sinaloa, Mexico

Melissa García-Carrasco
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

M. Gayathri
School of Biosciences and Technology, Vellore Institute of Technology, Vellore, Tamil Nadu, India

Souvik Ghosh
School of Biosciences and Technology, Vellore Institute of Technology, Vellore, Tamil Nadu, India

Mario Armando Gómez-Favela
Polytechnic University of the Sea and Mountain, La Cruz, Sinaloa, Mexico

Daniel Guajardo-Flores
Tecnologico de Monterrey, School of Engineering and Science, Monterrey, NL, Mexico

Erick P. Gutiérrez-Grijalva
Cátedras CONACYT—Research Center for Food and Development, AC, Culiacán, Sinaloa, Mexico

J. Basilio Heredia
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Daniel A. Jacobo-Velázquez
Tecnologico de Monterrey, The Institute for Obesity Research; Tecnologico de Monterrey, Escuela de Ingeniería y Ciencias, Zapopan, JAL, Mexico

Luis Alfonso Jiménez-Ortega
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Angel Licea-Claverie
Centro de Graduados e Investigación en Química, Tecnológico Nacional de México/ Instituto Tecnológico de Tijuana, Tijuana, Baja California, Mexico

Mariana Martínez-Ávila
Tecnologico de Monterrey, School of Engineering and Science, Monterrey, NL, Mexico

Luis Aurelio Montoya-Inzunza
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Melissa Moreira-Rodríguez
Tecnologico de Monterrey, Escuela de Ingeniería y Ciencias, Monterrey, NL, Mexico

Ulises Osuna-Martínez
Facultad de Ciencias Químico Biológicas, Universidad Autónoma de Sinaloa, Culiacán, Sinaloa, Mexico

Lorenzo A. Picos-Corrales
Facultad de Ingeniería Culiacán; Facultad de Ciencias Químico Biológicas, Universidad Autónoma de Sinaloa, Culiacán, Sinaloa, Mexico

Manuel A. Picos-Salas
Research Center for Food and Development, Culiacan, Sinaloa, Mexico

Jose P. Ruelas-Leyva
Facultad de Ciencias Químico Biológicas, Universidad Autónoma de Sinaloa, Culiacán, Sinaloa, Mexico

David Ulises Santos-Ballardo
Polytechnic University of Sinaloa, Mazatlán, Sinaloa, Mexico

Juan I. Sarmiento-Sánchez
Facultad de Ingeniería Culiacán, Universidad Autónoma de Sinaloa, Culiacán, Sinaloa, Mexico

Shreya Vinit Teredesai
School of Biosciences and Technology, Vellore Institute of Technology, Vellore, Tamil Nadu, India

Arturo Zizumbo-Lopez
Centro de Graduados e Investigación en Química, Tecnológico Nacional de México/ Instituto Tecnológico de Tijuana, Tijuana, Baja California, Mexico

CHAPTER 2

Diseases with the highest mortality

Sara Aviles-Gaxiola[a], Marilyn S. Criollo-Mendoza[a], Melissa García-Carrasco[a], Erick P. Gutiérrez-Grijalva[b], Israel García-Aguiar[c], and J. Basilio Heredia[a]

[a]Research Center for Food and Development, Culiacan, Sinaloa, Mexico
[b]Cátedras CONACYT—Research Center for Food and Development, AC, Culiacán, Sinaloa, Mexico
[c]Universidad Autónoma de Occidente, Unidad Regional Culiacán, Boulevard Lola Beltrán, Culiacán, Sinaloa, Mexico

Contents

2.1 Introduction

Noncommunicable diseases (NCDs) are the main cause of death today, and according to the World Health Organization (2021a, b, c, d), they are responsible for around 71% of all registered deaths worldwide, which are mostly described as premature diseases (Malta et al., 2017). They are also known as chronic diseases. Although genetic factors influence, they are mainly considered "lifestyle diseases" because they occur mostly because of personal habits and choices (Patel and Webster, 2016). NCDs were first recognized as a global problem in 2012 in the 65th World Health Assembly, where commitments were established to reduce the number of deaths caused by these diseases (Islam et al., 2014).

The most deadly NCDs are (1) cardiovascular diseases (CVDs), mainly ischemic heart disease and stroke, (2) chronic obstructive pulmonary disease, (3) a few types of cancers, (4) Alzheimer´s disease and other dementia, and (5) diabetes mellitus (Fig. 2.1) (World Health Organization, 2021a, b, c, d). As for

Phytochemical Nanodelivery Systems as Potential Biopharmaceuticals
https://doi.org/10.1016/B978-0-323-90390-5.00001-3

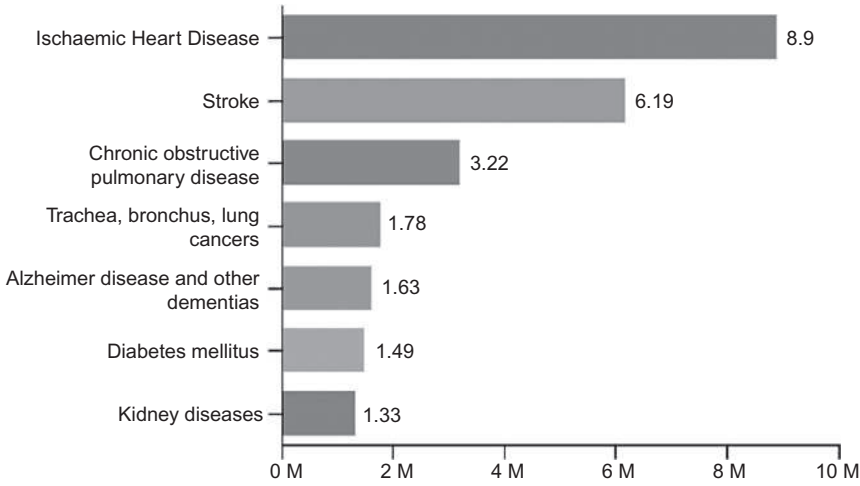


Fig. 2.1 The most mortal noncommunicable diseases. According to the WHO (2020), 7 of the 10 deaths in 2019 were because of noncommunicable diseases, which accounted for 74% of total deaths worldwide in this year.

CVD, chronic obstructive pulmonary disease, and some cancers (trachea, bronchus, and lung), the latest report generated by the World Health Organization (2020) indicates that these diseases have caused 15, 3, and 1.8 million deaths worldwide, respectively. In addition, the World Health Organization (2021a, b, c, d) estimated that 1.6 people died directly because of diabetes mellitus and that other 2.2 million people died because of high blood glucose. As for dementia and other mental diseases, the exact number is not known. However, 2.4 million deaths were associated with them in 2016 (Nichols et al., 2019).

NCDs attain both developed and developing countries (Yach et al., 2004). Although communicable diseases were the leading cause of death in developing countries, NCDs now have the highest mortality rate (World Health Organization, 2020).

The number of deaths because of NCDs is expected to increase over the years because of the continuous exposure to risk factors such as diet with high fat and calories, tobacco and alcohol abuse, and physical inactivity, among others (Gowshall and Taylor-Robinson, 2018).

2.2 Epidemic transition and increasing trends of noncommunicable diseases

For years, communicable diseases were the main cause of death globally. Nevertheless, according to the World Health Organization (2020), causes

such as the human immunodeficiency virus and tuberculosis are dropping out of these lists, and diseases such as diabetes and dementias are entering. Thus, although in 2010 6 of the 10 top causes of death worldwide were communicable diseases, nowadays, the number has lowered to 3 (Akselrod et al., 2019; Unwin and Alberti, 2006). An important reason for communicable diseases dropping in the number of deaths is that science has made a great deal of progress against infectious diseases (Islam et al., 2014).

On the other hand, NCDs pose a burden worldwide, both economic and social. This burden increase is alarming, especially for low-middle-income countries, where almost three-quarters of deaths occur (Lisy et al., 2016). Deaths associated with CVDs are currently the most worrying because certain risk factors are rising. These risk factors are mainly associated with the urbanization and industrialization aspects of developing cities (Negi et al., 2016). An epidemiological study suggests that following the same habits of life by 2025, many more people will be dying prematurely 10–15 years earlier because of NCDs in low- and middle-income countries (Sacco et al., 2016).

The main cause of increasing numbers of NCDs in developing countries is changing the previous lifestyle and introducing junk food. Although these habits are "old" for developed countries, people are now more aware of the risks and have better health care systems (Budreviciute et al., 2020).

As for overweight and obesity, it has been expanded dramatically in almost all developing and developed countries, reaching alarming levels of the adult population in industrialized countries (Agha and Agha, 2017). For example, the global prevalence of overweight and obesity has increased by 27% in adulthood during the past decades. Moreover, obesity represents a risk factor for many NCDs, most notably diabetes mellitus (type 2), hypertension, CVD, Alzheimer's disease, and even cancer (Avgerinos et al., 2019).

New data from the World Health Organization (2021a, b, c, d) estimate that the probability of dying from any major NCDs between the ages of 30 and 70 ranges from 10% in developed countries to 40% in developing countries.

2.3 Common risk factors

2.3.1 Noncommunicable diseases

2.3.1.1 Cardiovascular diseases

According to the WHO, CVDs are the major cause of death worldwide. It has been estimated that nearly 17.9 million people die of cardiovascular pathology each year. Some of the most common CVDs are coronary

heart disease, cerebrovascular disease, and rheumatic heart disease. In addition, CVDs are also one of the leading causes of premature death within the adult population (World Health Organization, 2021a, b, c, d). Several factors have been reported as risk factors of CVDs, and most of them are related to lifestyle. For instance, unhealthy diet, physical inactivity, tobacco use, and harmful use of alcohol, among others, are the main leading causes of CVDs. Also, pre-existing conditions such as hypertension and type-2 diabetes might increase the incidence of CVDs as raised blood pressure, raised blood glucose, raised blood lipids, overweight, and obesity are considered by the World Health Organization (2021a, b, c, d) as "intermediate risk factors" for CVDs and other complications. Moreover, noncommunicable diseases such as CVDs increase health care household costs, thus preventing poverty reduction.

The prevalence and number of deaths caused by CVDs are steadily increasing. For instance, from 1990 to 2019, the occurrence of CVDs rose from 271 to 523 million. Similarly, deaths caused by CVDs augmented from 12.1 to 18.6 million in the same year range (Roth et al., 2020). In this sense, the countries with the highest number of deaths associated with CVDs by 2020 are China, India, the Russian Federation, the United States of America, and Indonesia (Roth et al., 2020).

Globally, the main CVDs are ischemic heart disease, ischemic stroke, intracerebral hemorrhage, and hypertensive heart disease. These diseases are often attributed to metabolic, environmental, and behavioral risks; the most common are high systolic blood pressure, dietary risks, high low-density lipoprotein cholesterol, air pollution, a high body mass index, tobacco, high fasting plasma glucose, kidney dysfunction, harmful use of alcohol, and physical inactivity (Arnett et al., 2019; Roth et al., 2020).

CVDs are a group of noncommunicable diseases that are increasingly affecting the worldwide population with health and economic burdens in people from low-income countries that often lack appropriate therapeutic drugs. One of the main modifiable risk factors to prevent the onset of CVDs is incorporating a healthy lifestyle. This includes a nutritious diet, regular physical activity, caloric restriction (in the case of adults with overweight and obesity), and avoiding tobacco use and the harmful use of alcohol (Arnett et al., 2019).

Ischemic heart disease is the leading cause of death among CVDs. Reports have stated a prevalence of 178–220 million cases of ischemic heart disease in 2019 and are considered a threat to public health (Nowbar et al., 2019; Roth et al., 2020). It has also been reported that ischemic heart

disease represents around one-third of female deaths. Moreover, gestational diabetes mellitus increases the risk of ischemic heart disease and type-2 diabetes, considered a major problem in countries of all incomes (Daly et al., 2018; Nowbar et al., 2019). Although some of the main treatments for ischemic heart disease are related thrombolysis and percutaneous coronary interventions, studies focus on improving preventive and therapeutic drugs, with some related to mitochondrial dysfunction (Walters et al., 2012).

On the other hand, according to the Centers for Disease Control and Prevention, "ischemic stroke happens when blood flow through the artery that supplies oxygen-rich blood to the brain becomes blocked." Intravenous alteplase is one of the most efficient treatments for ischemic stroke, the most common stroke (Centers for Disease Control and Prevention, 2021; Virani et al., 2021).

Moreover, another type of stroke is hemorrhagic stroke, which happens when a brain artery leaks blood. The artery rupture increases the pressure on brain cells, causing damage. In this sense, intracerebral hemorrhage is the most common, and it occurs when a brain artery ruptures and the adjacent tissue is surrounded by blood (Centers for Disease Control and Prevention, 2021). The medical treatment for intracerebral hemorrhage includes anticoagulant and antiplatelet agents (Hemphill et al., 2015). Finally, hypertension is a public health problem associated with other comorbidities such as type-2 diabetes and CVDs. In this sense, hypertensive heart disease combines anomalies such as left ventricular hypertrophy, systolic and diastolic dysfunction, arrhythmias, and symptomatic heart failure. It is caused by the thickening of the left ventricle that causes hypertensive heart disease by elevated blood pressure (Drazner, 2011).

2.3.1.2 Cancer

According to the International Agency for Research on Cancer (2020), cancer is the second global cause of death, causing slightly more than 9.9 million deaths in 2020. The most common cancers in women are breast, colorectal, thyroid, cervical, and uteri, whereas in men, they are prostate, colorectal, lung, bladder, and stomach. Lung, colorectal, liver, stomach, and breast are the cancers with the most attributed deaths with 1.79 million, 935,173, 830,180, 768,793, and 684,996 deaths registered, respectively (Fig. 2.2) (Kim et al., 2018).

For more than half a century, the different causes of cancer have been studied. One of the first observations was that people's environment affected the development of this disease and the specific type of it (Blackadar, 2016).

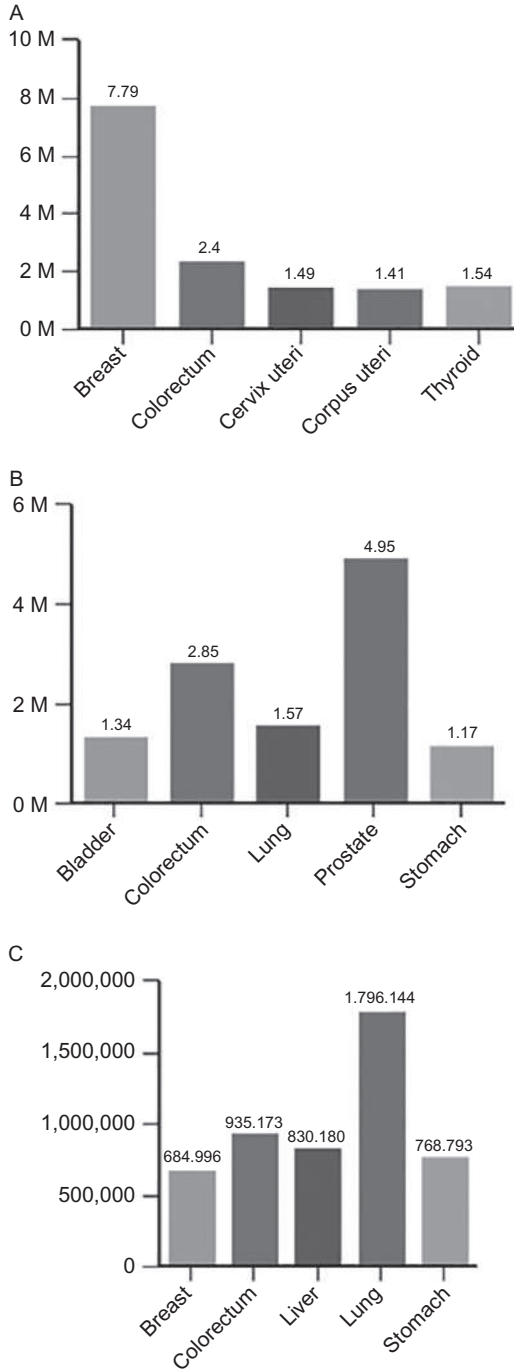


Fig. 2.2 The deadliest cancers. According to the International Agency for Research on Cancer (2020), cancer is the second cause of death globally causing slightly more than 9.9 million deaths in 2020. (A) Estimated number of incident cancer cases in women worldwide. (B) Estimated number of incident cancer cases in men worldwide. (C) Estimated number of deaths in both sexes worldwide.

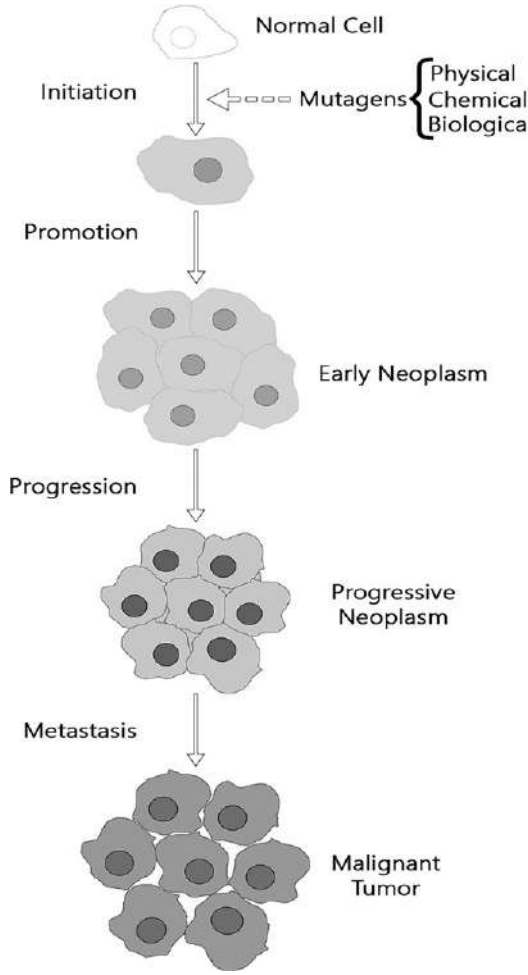


Fig. 2.3 Carcinogenic process development.

Carcinogenic process development occurs in three stages: initiation, promotion, and progression (Fig. 2.3). In the initiation stage, important signaling pathways are deregulated, such as proliferation or cell death; this is because of mutations in key genes such as tumor suppressor genes or proto-oncogenes; these mutations can occur spontaneously or induced by carcinogens. During the promotion stage, the genetically altered cells in the first stage proliferate, resulting in clonal expansion and reaching a critical size. Finally, in the progression stage, genetic instability grows, final neoplastic transformation occurs, and the tumor size increases (Salehi et al., 2018).

A vast investigation has been performed to identify the causes and control the appearance of the many different cancers to reduce their incidence. The main risk factors are alcohol and tobacco use, smoke from cooking, poor diet, lack of exercise, and air pollutants. These factors are also common to other NCDs. For example, tobacco use and air pollutants are related to chronic respiratory diseases, whereas poor diet and the lack of physical activity are associated to diabetes. Risk factors not associated with other NCDs are UV radiation overexposure and infections. The latter mainly includes hepatitis B and C viruses, which may promote liver cancer, human papillomavirus associated with cervical cancer, and *Helicobacter pylori*, which is a risk factor to stomach cancer (Gelband and Sloan, 2007). The deadliest cancers are described in depth below.

Lung cancer

Lung cancer was responsible to the most deaths worldwide in 2020. It is a very invasive cancer, and one of the reasons for its high mortality is that almost all patients (above 70%) diagnosed with lung cancer are in stage III or IV, where symptoms such as hemoptysis, cough, and weight loss start (Myers and Wallen, 2020). Lung cancer's main risk factor is smoking. In fact, most patients with this disease have been smoking for 20 years or more (Volk et al., 2020).

For its anatomic location, lung cancer is classified as adenocarcinomas (in peripheral bronchi, being mainly diagnosed in smokers and nonsmokers), squamous cell lung cancers (in main bronchi and linked to a history of smoking), small-cell lung cancers (submucosal lymphatic vessels and regional lymph nodes), and large-cell anaplastic carcinomas (appears in any part of the lung), and they are responsible for 40%, 30%, 15%, and 10% of all lung cancer cases, respectively (Lemjabbar-Alaoui et al., 2015). Lung cancer is mainly divided into two, small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC), which includes adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma (Zappa and Mousa, 2016).

As for NSCLC, it is often asymptomatic in stage I, and the recommended procedure is surgery, either lobectomy or pneumonectomy that shows a survival rate of around 78%. The survival rate is from 36% to 46% in stage II. Here, the preferred treatment is surgery, followed by chemotherapy and adjuvant therapy. However, in stages III and lV, lung cancer is considered incurable because the rate of survival of 5 years is 1%–3% (Siddiqui and Siddiqui, 2020). As for SCLC, it is very sensitive to chemotherapy, but it has a high recurrence rate (Asai et al., 2014). SCLC is divided mostly into

two stages: limited stage and extensive stage. The limited stage is characterized by cancer only on one side of the chest. It is usually treated with a radiation field. As for the extensive stage, it means that cancer spreads from one lung to the other (Kalemkerian et al., 2013).

Currently, many research groups are focused on studying the origin of aberrant signaling in lung cancer; recent studies have suggested that vaccination against influenza may provide clinical benefits, including reduced hospitalization and reduced mortality, to patients with lung cancer. A better understanding is needed, but some antiviral treatments or influenza vaccination could probably be recommended as an adjuvant to all patients with lung cancer (Angrini et al., 2021).

Colorectal cancer

Although in 1950 colorectal cancer (CRC) was rare, according to the World Health Organization (2021a, b, c, d), it is the second most mortal, with 935,173 deaths reported in 2020. It is the third most common cancer, with 1.93 million cases diagnosed. This increase is because of a change in lifestyle, mainly in poor dietary habits, obesity, alcohol intake, and smoking (Johnson et al., 2013). The specific health status increases CRC risk, such as having colitis and being obese (Park et al., 2012). On the other hand, the risk may decrease by up to 10% by the daily consumption of certain food, 10 g fiber and 200 mL milk, and also a daily physical activity for at least 30 min (Dahm et al., 2010; Song et al., 2015).

The relationship between risk factors and CRC is so high that 70% of the cases are sporadic because of somatic mutations linked to environmental factors. The rest of the cases are related to familial clustering (20%) and inherited syndromes, mostly familial adenomatous polyposis and lynch syndrome (10%) (Recio-Boiles et al., 2019). Lynch syndrome is caused by a mutation in mismatch DNA repair genes: EPCAM, PMS2, MSH2, MSH6, and MLH1, which promote the accumulation of mutations in DNA. On the other hand, adenomatous polyposis is caused by mutations in the APC gene. This gene controls the activity of the Wnt signaling pathway (Schreuders et al., 2015).

CRC may be classified according to stages, going from stage 0 to stage IV. In stage 0, cells with mutations are found in the innermost layer of the colon wall, known as mucosa. In stage I, these cells have spread to the next layer, the submucosa. In stage II, these cells have crossed the colon wall's muscle layer, and in stage III, the cells have been spread to nearby lymph nodes. Finally, in stage V, they have spread to other body parts (Board, 2019).

CRC management will depend on the stage of the disease (Tortora and Derrickson, 2018). The most used treatment for CRC is surgery, either alone (in early stages) or accompanied by adjuvant therapy. Surgery is applied alone from stage 0 to stage II, and the method used will depend on the disease progression (Wolpin and Mayer, 2008). Local excision is applied when cancer is found only as a polyp and no cutting through the abdominal wall is needed; instead, a tube with a cutting tool is passed through the rectum by a polypectomy process. Whenever cancer progression is more spread, a part of the colon or all of it is removed by a process called resection, either by anastomosis or by colostomy. Although the colon is brought back together in the first one, this is not possible in colostomy, and a stoma is made on the outside of the body for a waste exit. Subsequently, an anastomosis is performed (Matsuda et al., 2016). The resection can be right, left, or total, depending on the tumor localization. Surgery is considered a safe process, and with laparoscopy, a minimally invasive technique, the postoperative pain is less, and the recovery time is shorter. For stage III and high-risk stage II patients, adjuvant chemotherapy is necessary. Until the 1990s, 5-fluorouracil was practically the only chemotherapeutic agent for CRC treatment. Over the past 20 years, six new chemotherapeutic agents have been introduced: irinotecan, capecitabine, oxaliplatin, cetuximab, bevacizumab, and panitumumab (Baek et al., 2019). Colorectal cancer prognosis depends upon the stage when the diagnosis is made. The earlier the stage, the higher the possibilities of survival (Haggar and Boushey, 2009).

On the other hand, the significant difference in gut microbiota composition between cancer patients and healthy individuals demonstrates diagnostic and prognostic potentials of special microbial pathogens in cancer, with several studies supporting the assumption that fecal microbiota transplantation could harbor a potential therapeutic ability for CRC (Chen et al., 2019).

Liver cancer

According to the World Health Organization (2021a, b, c, d), in 2020, lung cancer caused 830,130 deaths from 905,677 diagnosed cases, being the sixth most diagnosed cancer worldwide. It is the third most mortal cancer. Diverse risk factors have been associated with it, being recognized as strong chronic hepatitis B and C viruses, smoking, and alcohol abuse. As for alcohol use, cirrhosis increases the risk of liver cancer. Another important risk factor is exposure to aflatoxin in corn-based products (Recio-Boiles and Babiker, 2021). Therefore, given the risk factors associated with

hepatocellular carcinoma, prevention is more associated with no alcohol and cigarette consumption. Nevertheless, the other risk factors are not easy to control, so it is recommended for patients with hepatitis infections and cirrhosis for periodic ultrasonography examination in order to detect the disease early. Also, the measurement of α-fetoprotein is a common practice in detecting liver cancer (Tsukuma et al., 2005).

Liver cancer stages go from I to IV. A single tumor, known as a primary tumor, has not spread in stage I. It can be of any size. There is more than one tumor in stage II, and they may have been grown into blood vessels. In stage III, the tumors have grown into the other covering of the liver, and in stage IV, it has spread to nearby lymph nodes and may have extended to other organs (Chen et al., 2014).

A liver transplant or a resection surgery is the most effective treatment for liver cancer. Nevertheless, only 30% are candidates for these procedures, whereas 70% should be treated differently by local ones, for example, radiofrequency and transarterial chemoembolization (Chen et al., 2016). Sorafenib is used when there is an advanced disease, which is a single-agent multikinase inhibitor. Another option is a recombinant monoclonal antibody called ramucirumab, which inhibits vascular endothelial growth factor receptor 2 (Recio-Boiles and Babiker, 2021).

Stomach cancer

According to the World Health Organization (2021a, b, c, d), stomach cancer is the fourth most mortal with 768,793 deaths reported and is the fifth most common cancer worldwide, with around 1.1 million cases diagnosed in 2020. The main risk factors are an unhealthy diet, especially the consumption of N-nitrose compounds, high-salt food, a low vitamin C and A diet, smoking, drinking contaminated water, and smoked foods (Brenner et al., 2009). Other risk factors are *Helicobacter pylori* infection, Epstein-Barr virus infection, and occupational exposure to metal, coal, and rubber manufacturing (Singh and Jha, 2017). Also, to a less extent however, other risk factors are radiation exposure and gastric surgery. Meta-analyses have shown that the consumption of certain food may reduce the risk of having stomach cancer, for example, fiber, fruits, and vegetables (Hu et al., 2015). Similar to colonic cancer, most stomach cancers are sporadic; 10% are associated with family history, and up to 5% of hereditary familial gastric cancers are associated with syndromes such as gastric adenocarcinoma and proximal polyposis of the stomach (Recio-Boiles and Babiker, 2020).

The stages of stomach cancer go from I to IV. In stage I, tumors are found in the stomach lining, and in stages II and III, they spread into stomach layers and are near lymph nodes. As for stage IV, cancer has spread to distant lymph nodes and other parts of the body. The outcome of the disease depends on the tumor extent. When it is localized, 50% of patients, or even more, are cured. However, when it is not, the survival rate goes from 10% to 20% (Screening and Board, 2020). Surgery is the main therapy for gastric cancer, but chemotherapy and chemoradiation are recommended to extend to lymph nodes. Cisplatin and fluoropyrimidine are the used chemotherapy drugs (Orditura et al., 2014).

In recent years, there has been a better understanding of the molecular mechanisms associated with the pathogenesis and biology of stomach cancer. The identification of biomarkers related to the prognosis and treatment of stomach cancer has been achieved. Despite this, up to now, few targeted options have been approved for the treatment of metastatic stomach cancer. The first target agent approved for stomach cancer is the anti-human epidermal growth factor receptor-2 drug trastuzumab. In contrast, the antiangiogenic drug ramucirumab has received approval in the second-line setting as a monotherapy or combined with paclitaxel. More recently, agents such as nivolumab and pembrolizumab have been approved for patients with heavily pretreated advanced gastric cancer. Recent advances in the molecular characterization of stomach cancer have broadened the knowledge. It will serve to develop new treatment options that increase the survival rates of patients diagnosed with metastatic stomach cancer (Pellino et al., 2019).

Breast cancer

According to the World Health Organization (2021a, b, c, d), it is the fifth most mortal cancer with 684,996 deaths and the most diagnosed one with 2.2 million cases in 2020. Breast cancer risk factors are gender, age, personal history, family history, exogenous hormone use, and histologic risk factors such as atypical tissue and lobular carcinoma in situ. As for the first one, most cases occur in women. Only 10% of all breast cancer cases are associated with genetic factors. The most commonly mutated genes are BRCA1 and BRCA1 (Alkabban and Ferguson, 2019).

The main strategies to reduce breast cancer incidence are avoiding exogenous hormones, tobacco, alcohol, and radiation exposure. Also, maintaining a normal weight and physical activity is recommended. A mastectomy or a bilateral oophorectomy is suggested whenever there is a family or personal history (Sauter, 2018).

Breast cancer stages go from 0 to IV. In stage 0, there is noninvasive cancer localized in the breast tissue. In stage I, there are already cells invading the surrounding tissue. In stage II, it is found in lymph nodes, and in stage III, it is near the breastbone. Finally, in stage IV, it spreads to other organs, most commonly the lungs. When the cancer is early, the patients may have breast-conserving surgery, radiotherapy, or mastectomy; here, the tumor is removed (Iqbal et al., 2015).

When there is already invasive cancer, adjuvant chemotherapy is needed. It can be oral or bloodstream chemotherapy. The most used drugs are doxorubicin, epirubicin, paclitaxel, docetaxel, and 5-fluorouracil. These drugs are usually combined during systemic treatment (Taher et al., 2016).

Triple-negative breast cancer (TNBC) is the most aggressive subtype. TNBC is a genetically diverse, highly heterogeneous, and rapidly evolving disease that challenges the possibility of individualizing treatment. The standard frontline chemotherapy, composed of anthracyclines, alkylating agents, and taxanes, is commonly used to treat high-risk and locally advanced TNBC. Several Food and Drug Administration (FDA)-approved drugs such as Keytruda, Tecentriq, and Trodelvy have shown promise in improving clinical outcomes for TNBC (Gupta and Collier, 2020). Otherwise, several epidemiological studies have indicated the inverse correlation between the intake of whole grains and the incidence of breast cancer. Whole grains are important food sources of phytochemicals, which have well-defined roles in managing each stage of breast carcinogenesis, suggesting that the consumption and development of nutraceuticals such as whole grain phytochemicals could reduce breast cancer risk (Xie et al., 2019).

2.3.1.3 Respiratory diseases

Asthma

It is a common chronic respiratory disease that affects between 1% and 18% of the population of various countries; it has a global prevalence ranging from $<5\%$ to $\geq 20\%$ in adolescents and an estimated 8.6% in adults (The Global Asthma Report, 2018). Among its main characteristics are inflammation of the airways and variable limitation of expiratory airflow. Some disease symptoms are wheezing, dyspnea, chest tightness, and cough (Jiang et al., 2021).

Genetic and environmental factors drive both the origin and severity of this disease. Most cases of asthma start during childhood in association with immunoglobulin E (IgE)-dependent sensitization to common environmental allergens (Custovic, 2015). However, it can also arise during adult life.

In this case, it usually occurs in the absence of any allergy. However, it is generally accompanied by intolerance to nonsteroidal anti-inflammatory drugs (NSAIDs), rhinosinusitis, and nasal polyps (Amelink et al., 2013).

Risk factors for this disease can be prenatal, such as ethnic origin, cesarean delivery, and a mother smoking during pregnancy, as well as postnatal, which include high home levels of endotoxins and allergens, viral and bacterial infections, air pollution, use of antibiotics, exposure to paracetamol, and obesity (Belsky and Sears, 2014).

It is important to mention that asthma is often accompanied by comorbidities, including nonallergic disorders, such as obesity, gastroesophageal reflux, and psychiatric conditions. Also, asthma is subject to periods of rapid deterioration caused by high exposure to allergens, air pollutants, and certain medications such as aspirin and other NSAIDs (Holgate et al., 2015).

Inflammation of the airways is the main characteristic of asthma. T helper 2 (Th2) inflammation (allergic and eosinophilic phenotypes) occurs in 80% of children and most adults with asthma, along with sensitization to environmental allergens, such as dust mites, fungi, and pollen (Permaul et al., 2012). In addition, this sensitization is associated with some other clinical manifestations such as atopic dermatitis (eczema), allergic rhino-conjunctivitis, and food allergy (Bantz et al., 2014). The inflammatory infiltrates accompanying Th2 lymphocyte responses are mainly composed of eosinophils, including mast cells, basophils, neutrophils, monocytes, and macrophages. Mast cell degranulation and eosinophil vacuolation show cell activation and the release of inflammatory mediators in asthma; most of the mucosal mast cells in mild to moderate allergic asthma are of the type that expresses cell-dependent tryptase, whereas in the more intractable forms of asthma, mast cells that contain both tryptase and chymase, which are more dependent, predominate the stem cell factor (also known as KIT ligand) (Holgate et al., 2015).

Asthma has been commonly classified according to the severity of the symptoms or the degree of control of the disease. According to Wenzel (2012), certain asthma phenotypes have been identified from recognizable groups of demographic, clinical, and pathophysiological characteristics, such as allergic, nonallergic, late-onset, fixed airflow obstruction, obesity-induced asthma, and electronic nose-derived inflammatory phenotypes. Furthermore, some types of asthma can go into spontaneous remission; for example, during late childhood and adolescence, they can also respond to allergen-specific immunotherapy by acquiring immune tolerance (Fu et al., 2014).

For the treatment of this disease, a variety of drugs have been used, including inhaled corticosteroids (ICS), long-acting β2 adrenergic receptor agonists (LABAs), long-acting muscarinic antagonists, leukotriene receptor antagonists (LTRAs), and for more severe disease the IgE-specific monoclonal antibody omalizumab (Holgate et al., 2015). Although the staggering diagnosis for disease detection and treatment has these, treatments have been shown to alter the natural history of the disease. The above is known for cluster analysis and reduced dependence on short-acting inhaled bronchodilators (SABAs). No other nonhierarchical analyses have elucidated asthma subtypes associated with different causal pathways, natural histories, and responses to interventions (Moore et al., 2010).

On the other hand, the disease can be controlled in almost all mild and moderate asthma patients using standard inhaled treatments. However, between 5% and 10% of patients experience subtypes of asthma that are difficult to treat and poorly controlled (Heffler et al., 2019). Among these, one of the most relevant is severe asthma, which, according to the European Respiratory Society as well as the American Thoracic Society, is a condition that can only be controlled by high doses of inhaled corticosteroids (ICSs) and long-acting β2 adrenergic agonist (LABA) combinations, which may require other drugs (for example, tiotropium, leukotriene modifiers, and oral corticosteroids). Severe asthma patients are characterized by urgent medical needs and may be eligible for complementary biological therapies (Siddiqui et al., 2019). Biological therapies consist mainly of licensed monoclonal antibodies that target specific molecules involved in the pathobiology of eosinophilic, allergic, and nonallergic asthma type 2 (T2-high), including IgE, interleukin-5 (IL-5) and its receptor, and interleukin-4 (IL-4); there are also experimental biological products that target innate upstream cytokines, such as thymic stromal lymphopoietin (TSLP) (Al-Sajee et al., 2018; Nakajima et al., 2020).

As biochemical messengers of immune cells, cytokines play an important role in regulating allergic inflammation as asthma, characterized by hyper-responsiveness and reversible airway obstruction, recruitment of inflammatory cells, and excessive production of mucus. Therefore, plant-derived extracts and related active compounds have potential therapeutic activity for treating asthma by modulating the release of proinflammatory and anti-inflammatory cytokines and suppressing inflammatory cell accumulation (Gandhi et al., 2020). For example, the methanolic extract of *Moringa oleifera* leaf has beneficial effects against bronchoconstriction, airway inflammation, and asthma (Suresh et al., 2020). However, further

exploratory studies are needed to identify and isolate other potential antiasthmatic candidate molecules from other plants.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a multifactorial disease that occurs more commonly because of inflammatory processes and is mainly caused by cigarette smoking or inhalation of harmful gases or granules. It is also known that even when people with this disease stop smoking, a continuous cycle of inflammation can cause a unceasing decline in lung functions (Morse and Rosas, 2014). It is believed that COPD can become the third leading cause of death worldwide. This common respiratory disease is not completely reversible and develops progressively, and it is characterized by airflow blockage and respiratory-related actions, emphysema and chronic bronchitis, and airflow limitation (Yang et al., 2021).

Inflammatory cells play a very important role in the development and progression of the disease. Neutrophils and macrophages release proteolytic enzymes and generate oxidants, causing tissue damage; neutrophils are the predominant cells in the conducting airways, whereas macrophages are predominant in the secretions of the small airways and the parenchyma. Besides, the neutrophils of the airway tissue increase during infection and exacerbations. In contrast, the number of parenchymal neutrophils is inversely related to the destruction of the alveolar wall, the reason why it is believed not to participate in the progression of emphysema. On the other hand, macrophages increase throughout the lumen and epithelium of the airways, which is related to the severity of the disease, airway obstruction, and the degree of alveolar wall damage in emphysema. In the case of cytokines and chemokines, these can enhance inflammation and trigger an immune response. The CD8+ suppressor/cytotoxic T lymphocytes release cytotoxic perforins and granzyme B that cause cell death and apoptosis, one of the main characteristics of emphysema. In addition, during COPD, there is an increase in the CD8+/CD4+ ratio of T cells, or the total number of CD8+ and CD4+ T cells, in the tissue. Factors such as smoking, smoking history, degree of airway obstruction, and emphysema are related to increased CD8+ cells and the CD8+/CD4+ ratio (Tetley, 2005).

Tantucci (2021) suggests that it should be understood that the acronym COPD does not refer to a single disease but encompasses a functional respiratory disorder characterized by a chronic, irreversible, and naturally progressive maximum reduction of airflow, which can be the result of two

different initial pathologies, namely, chronic fibrosing bronchiolitis and panlobular pulmonary emphysema.

The diagnosis of COPD must be made according to risk factors, the patient's medical history, physical examination, and spirometry. Subsequently, the prevalent underlying disease must be determined through more detailed functional tests and sometimes imaging techniques, in addition to quantifying its severity using a multiparametric evaluation, where not only the degree of functional deterioration but also chronic symptoms, physical performance, nutritional status, and deterioration of gas exchange (Divo et al., 2012) should be included. It is also important to identify the presence of more relevant comorbidities, which should be investigated along with a history of previous acute exacerbations of COPD (Wedzicha et al., 2013). Besides, the determination of recognized biomarkers of low-grade systemic inflammation, such as plasma CRP (C-reactive protein) and fibrinogen, could be useful under stable clinical conditions because they significantly increase the risk of acute exacerbations and mortality in patients with COPD (Agustí et al., 2012).

Patients with COPD associated with chronic bronchiolitis can receive pharmacological treatment for the various components of airway obstruction, such as inflammation, subepithelial edema, increased broncho motor tone, bronchoconstriction, and accumulation of endoluminal mucus exudate. As for patients with COPD with the lack of alveolar insertions and the loss of lung elastic recoil, there is not an effective pharmacological treatment. Moreover, subepithelial fibrosis and peribronchiolar fibrosis are characteristics of the small airways that currently cannot be treated in chronic bronchiolitis. Therefore, drug therapy may be more effective when COPD is sustained by chronic bronchiolitis and certainly much less if emphysema is panlobular or tends to become centrilobular in the prevalent disease (Baldi et al., 2010).

From the above information, it is deduced that the drugs are much more useful in the mild to moderate stage of airflow obstruction in COPD, where chronic bronchiolitis and the natural loss of absolute lung functions largely predominate (Tantucci and Modina, 2012). In this sense, "the fundamental pharmacological treatment is represented by bronchodilators, long-acting and ultra-long-acting beta-2 selective adrenergic agonists (LABA or u-LABA) and long-acting and ultra-long-acting muscarinic receptor antagonists, and anticholinergic drugs (LAMA or uLAMA), topically administered by inhalation as a fine or ultrafine aerosol using different pressurized dosing dispensers (pMDI) or as fine or ultrafine dry powders using different

devices" (Tantucci, 2021). These can induce bronchodilation and decrease broncho motor tone, thus allowing a reduction in operative lung volume. Bronchodilators, however, can also improve mucociliary clearance differently and could exert an anti-inflammatory action by decreasing mechanical stress because of dynamic hyperinflation and repeated closure of small airways and reopening them during tidal breathing (Wedzicha et al., 2013).

Although vitamin D is best known for its role in bone homeostasis, it has recently gained attention because of its wide range of functions, including its immunomodulatory effect. Several lung diseases benefit from vitamin D supplementation. The evidence is compelling in adult vitamin D-deficient patients with COPD and may be transferred to clinical recommendations or guidelines. In addition, future studies should determine if vitamin D administration through inhalation may exert a more potent direct effect (Mathyssen et al., 2017).

Asthma and COPD are the most common chronic respiratory diseases (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Airflow obstruction is a common underlying condition responsible for clinical symptoms in both diseases. In the case of asthma, it is easily reversible spontaneously or with treatment; in COPD, however, it is persistent and progressive (Rogliani et al., 2016). In addition to this, inflammation of the airways contributes to the pathogenesis of both diseases. Therefore, the use of bronchodilators (β2-agonists, muscarinic antagonists, and theophylline) to decrease airway resistance and anti-inflammatory drugs [corticosteroids, leukotriene receptor (LT) antagonists, and phosphodiesterase (PDE) 4 inhibitors] for the treatment of chronic inflammation of the airways has become standard approaches in the treatment of asthma and COPD (Billington et al., 2017; Xing et al., 2020).

2.3.1.4 Diabetes

Diabetes mellitus is one of the metabolic diseases with the highest frequency and prevalence. It is a disease characterized by carbohydrate metabolism disorders with chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or a combination of both (Škrha, 2021). Diabetes prevalence and its specific complications make it one of the main social and health problems today. It is important to consider that diabetes mellitus is not an inert process, rather it is a disease in continuous evolution. Therefore, its severity can be maintained, improved, or worsened, mainly associated with the metabolic control of the natural history of the disease (Conget, 2002).

This disease's risk factors are an excess body weight, high blood pressure, age, and an unhealthy diet. In addition, diabetes treatment can cause various long-term complications, for example, CVDs such as hypertension, heart failure, and atherosclerosis and chronic kidney diseases such as nephropathy, retinopathy, and peripheral neuropathy, and it can also cause sexual problems in men and women (Kizilay et al., 2017; Singh et al., 2013).

Diabetes may be classified as type 1 and type 2, of which more information will be addressed in the next section. In Fig. 2.4, the two most common types of diabetes, its main feature, and complications of both types can be seen.

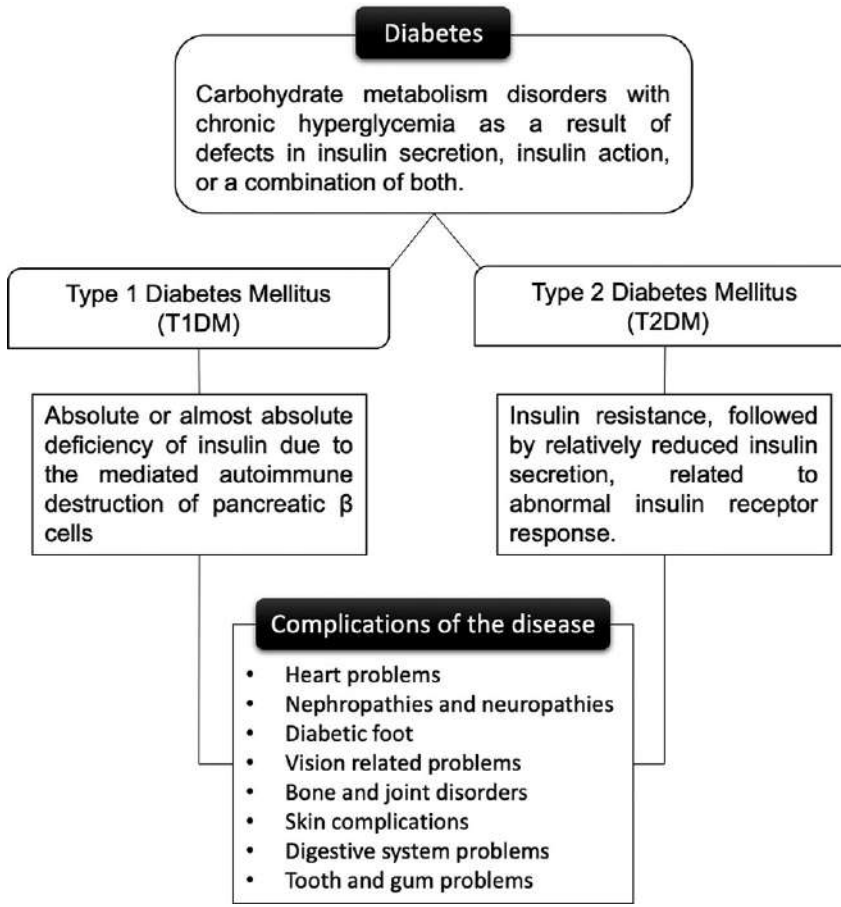


Fig. 2.4 Characteristics of the types of diabetes and complications of the disease.

Type 1 diabetes mellitus (T1DM)

T1DM is characterized by an absolute or almost absolute insulin deficiency because of the mediated autoimmune destruction of pancreatic β cells. This can occur at any age (Atkinson et al., 2014). Patients with T1DM have elevated plasma glucagon levels and low or absent insulin levels, and the remaining β cells cannot respond to insulin-secreting stimuli. In T1DM, the pancreas is reduced in size with exocrine atrophy, lymphocytic infiltration, fibrosis, and a lobular pattern of β cell destruction that increases with the duration of the disease (Atkinson et al., 2014). The presence of cells damaged by insulin infiltration is considered a histological hallmark of T1DM. Most patients (90% of people) with newly diagnosed T1DM have at least one or more autoantibodies early in the disease. Among the specific autoantibodies associated with this disease are glutamic acid decarboxylase (anti-GADA), insulin autoantibodies (IAA), insulinoma-associated autoantibodies 2 (IA-2A), cytoplasmic autoantibodies of the cells of islets (ICA), and zinc transporter eight autoantibodies (ZnT8A) (Ziegler and Nepom, 2010).

On the other hand, the human leukocyte antigen (HLA) complex, which represents an important component of the genetic risk, approximately 50%, plays a key role in the pathogenesis of T1DM. The major histocompatibility complex encodes the human leukocyte antigen (HLA) system. Autoantigens are presented on the b-cell surface by HLA class I molecules that are then presented to T cells by HLA class II molecules (Trowsdale and Knight, 2013). The autoimmune responses generated in T1DM elicit a chronic inflammatory state in β cells, resulting in protein misfolding, an altered redox state in the endoplasmic reticulum, and ultimately β cell apoptosis. Furthermore, the GRP78, insulin, and GAD65 proteins may undergo inappropriate post-translational modifications that represent neoantigens and, therefore, may induce β cell autoimmunity (Sherr et al., 2008).

This disease is a catabolic condition, and patients depend on exogenous insulin to prevent ketosis, decrease hyperglucagonemia, and normalize protein and lipid metabolism (Moin et al., 2021). Preservation of pancreatic β cell functions to maintain residual insulin production through C-peptide levels contributes to glycemic control and reduces the risk of complications associated with hyperglycemia (Sherr et al., 2008).

In several clinical trials, immunological approaches have been evaluated to prevent the progression of β cell loss after T1DM is diagnosed. These methods aim at chronic immunosuppression are addressed to maintain insulin production for some time after the diagnosis of the disease as well

as the induction of immune tolerance by eliminating autoreactivity, while modifying the autoimmune response so that continuous immune suppression is not necessary (Keymeulen et al., 2005). On the other hand, currently, the use of a combination of genetic and immune markers has greatly improved the prediction of the disease and decreased risk, for example, in a subgroup of people who have not yet met the criteria for the diagnosis of T1DM, but those who have a very high risk of developing the disease can be identified, and these can be considered with preclinical T1DM (Sherr et al., 2008).

Type 2 diabetes mellitus

Type 2 diabetes mellitus (DM2) is primarily characterized by insulin resistance, followed by relatively reduced insulin secretion, which is related to abnormal insulin receptor response. Although this type of diabetes represents the most common worldwide, in most patients, there has been evidence of "prediabetes" for many years before meeting the criteria for DM2 (Rahman et al., 2020). In this sense, prediabetes is known as impaired fasting glucose and impaired glucose tolerance, which can be reverted to normal through a series of precautions, for example, control of diet and selective application of drugs for better insulin sensitivity, and thus reduce the level of glucose production (Divella et al., 2016; Shlomai et al., 2016).

Among the factors associated with this disease are lifestyle (poor diet, obesity, lack of physical activity, and stress) and genetic factors. The latter considered the potential source of abnormalities in the islet β cell functions. Defective β cells lead to reduced insulin sensitivity and increased insulin resistance, causing a higher demand for insulin, a condition clinically known as hyperinsulinemia and presented during the prediabetic stage (Boura-Halfon and Zick, 2009; Murea et al., 2012). When the simultaneous production of the amyloid polypeptide is high and continues for a longer period, the formation of the amyloid islet is induced, which can cause degeneration of β cells. Continuous insulin resistance and reduced insulin secretion cause an enhanced response in normal β cells, which increase insulin and islet amyloid peptide levels. If left unchecked, cyclic events can lead to an increase in the level of amyloid and a decrease in the insulin production capacity of the pancreas. This insufficient insulin production induces an increase in serum glucose concentration. Therefore, amyloid polypeptide acts as an endogenous diabetogenic factor that leads to β cell dysfunction and abnormal insulin production (Rahman et al., 2020). For this reason, the control of DM2 can include prevention and control of the process of amyloid-related

β cell failure in the early stage to inhibit the overproduction of amyloid polypeptide from human islets (Potter et al., 2009; Rivera et al., 2014).

One of the pillars for the treatment of DM2 is dietary advice and changes to a healthy lifestyle. The American Diabetes Association recommends a hypocaloric diet for overweight or obese adults with DM2 to induce weight loss. Some studies suggest that a diet rich in monounsaturated fatty acids is associated with better glycemic control coupled with lifestyle changes, which can even prevent the onset of DM2 and its progression (Evert et al., 2013).

2.3.1.5 Neurogenerative diseases

Chronic degenerative diseases (CDDs) (Fig. 2.5) are those in which neuronal cells and dysfunction of the nervous system are progressively and gradually lost; currently, there are more than 500 neurological diseases, which occur more frequently in older adults. Among the most common diseases are Parkinson's (PD) and Alzheimer's (AZ) (Brown Rebecca et al., 2005; Hou et al., 2019; Kovacs, 2017; Pogacnik et al., 2020). Neurodegenerative diseases can be classified mainly into two types based on the determination of clinical symptoms: (a) given the region where the neuronal dysfunction is found and (b) by proteins present which show different biochemical modifications as well as their accumulation of these in intracellular (neurons) or extracellular spaces (Kovacs, 2018). Molecular studies carried out in patients suffering from this type of disease have shown the formation of protein deposits in the brain. Some of these proteins are amyloid-β (Aβ), α-synuclein, and hyperphosphorylated T (p-T) (Coulthard and Love, 2018; Kovacs, 2018). Structural deformations have also been detected. They occur long before any type of symptoms appear; also, environmental factors can cause the appearance of this type of disease (Bondi et al., 2017). In various studies, it has also been reported that oxidative stress plays an important role because it can produce reactive oxygen species (ROS) (which can cause a malfunction of the redox system). The brain is a vulnerable organ to this imbalance because of the high oxygen demand, producing cell lipid peroxidation (Kim et al., 2015a; Reed, 2011). Neuroinflammation, mitochondrial dysfunction, and brain cell autophagy have also been determining factors for CKD's appearance (Bolós et al., 2017; Nixon, 2013). Because these diseases are progressive, the used treatments are palliative. Within the new treatments that are being tested are gene therapy, herbal therapy, iron chelators, and nanotechnology, among others (Albarracin et al., 2012; Giacoppo et al., 2015; Hider et al., 2011; Maher, 2019; Maiti and Dunbar, 2018; O'Connor and Boulis, 2015; Solanki et al., 2016).

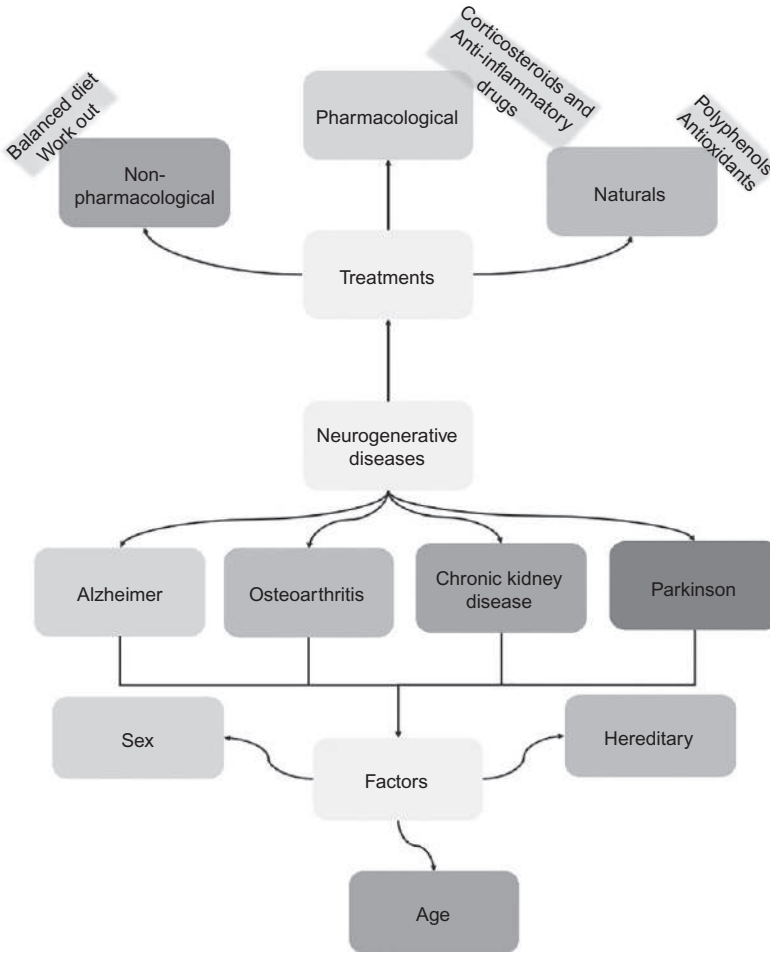


Fig. 2.5 The most common chronic degenerative diseases and their main risk factors and treatments.

Alzheimer (AZ)

AZ is the most common disease-causing dementia, and it does not have a cure to date. The deterioration of AZ patients increases twice every 5–10 years (Bolós et al., 2017; Godyń et al., 2016). The pathogenesis of this disease is not clear because the factors (genetic factors, cerebrovascular disease, traumatic brain injury, depression, hormonal disturbance, inflammation, and family health history, among others) that promote its appearance are very varied. AZ is characterized by the presence of extracellular neuritic (senile) plaques and intracellular neurofibrillary tangles. Senile plaques are

formed by the accumulation of amyloid-β protein in the extracellular space, whereas T-protein accumulates within neurons (Alzheimer's, 2019; Godyń et al., 2016).

This disease can be divided into three stages: (i) early, (ii) moderate, and (iii) late. Depending on the stage in which they are, the patients present different symptoms: memory loss, loss of their ability to speak, cognitive skill deterioration, and attention deficit, among others. In addition, little by little, they lose the ability to perform daily tasks such as bathing, going to the bathroom, cooking, and so on (Zvěřová, 2019). This diagnosis is usually based on the medical history, physical and neurological examinations, and neuroimaging (DeTure and Dickson, 2019). In some studies, it has been revealed that sex is a predominant factor for the appearance of this disease because it occurs with a higher prevalence in women; in addition to this, a decrease in different vitamins (C, E, B12, and B6) and homocysteine has also been found (Laws et al., 2018; Pike, 2017). Some of the processes involved in this disease are excitotoxicity, oxidative stress, calcium and metal dyshomeostasis, neuroinflammation, and mitochondrial damage (Alzheimer's, 2019; Chen and Zhong, 2014; Heneka et al., 2015; Kumar, Singh, and Ekavali, 2015). Currently, there are only six drugs approved by The US Food and Drug Administration (FDA) to treat AZ: rivastigmine, galantamine, donepezil, memantine, memantine combined with donepezil, and tacrine. These drugs help the formation of neurotransmitters (except memantine). The low number of available drugs is because of the rapid rate of degradation of the patient's health, so the researchers believe that studies should be carried out at the earliest stage of the disease and therefore have enough time to complete clinical studies (early detection of AZ can be performed with the help of biomarkers) to find the ideal treatments. There are also nonpharmacological treatments that can be used. These are mainly based on maintaining cognitive skills (computerized memory training, listening to favorite music to stimulate memory, and incorporating special lighting to mitigate sleep disorders).

As stated before, the intake of vitamins C, D, and E; omega-3 fatty acids; and ginkgo biloba helps prevent cognitive decline (Alzheimer's, 2019; Butler et al., 2017; Chen et al., 2018; DeMichele-Sweet and Sweet, 2010). However, because of the characteristics of this disease, various researchers have recommended looking for different treatments against it as it is the case of using gene therapy which consists of mutating genes present in other proteins such as the amyloid β-protein precursor, which will increase Aβ production or the $A\beta_{42}/A\beta_{40}$ ratio. Collectively, these discoveries provided

the essential connection between the long-known familial aggregation of early AZ onset and the increase in Aβ production observed in the brains of autopsied AZ patients, which originally gave rise to the "amyloid cascade hypothesis of AZ" (Bekris et al., 2011; Bertram and Tanzi, 2012). Another strategy that has been investigated later is the use of delivery systems (polymeric nanoparticles, carbon nanotubes, and nanofibers) that help to pass the cranioencephalic barrier and thus facilitate drug trafficking (Modi et al., 2010; Niu et al., 2019). Herbal therapy has also been considered; for instance, some byproducts of natural origin such as polyphenols (curcumin and resveratrol) have been be used. They have shown antioxidant effects, thus helping to reduce the presence of ROS and reduce oxidative stress as well as neuroinflammation (Hamaguchi et al., 2010; Maher, 2019; Maiti and Dunbar, 2018; Pohl and Kong Thoo Lin, 2018; Sawda et al., 2017).

Parkinson disease (PD)

PD is the second most common degenerative disease that is characterized by a movement disorder. The main symptoms of PD are bradykinesia, rigidity, and tremor, and with time, some mental symptoms also begin to appear. Like AZ, it occurs with a higher incidence in older people. This is characterized by presenting a-synuclein-containing Lewy bodies in the substantia nigra of the brain, which gets in the way of the interaction of dopaminergic neurons reducing the ability to control limb movements (Balestrino and Schapira, 2020; Dickson, 2018). The disease diagnosis is given mainly through the symptoms mentioned earlier; these can occur individually or together (Poewe et al., 2017; Rizek et al., 2016). The origin of this disease is unknown, but different genetic factors and the number of people in the same family suffering from the disease are relevant (Armstrong and Okun, 2020; Tysnes and Storstein, 2017). Also, environmental factors have been described. For example, exposure to certain chemicals such as 1-methyl-4-phenyl tetrahydropyridine, annonacin, manganese, trichloroethylene, and carbon monoxide can cause the death of a nigrostriatal cell, which is the mechanism responsible for the activation of factors associated with the onset of the disease (activation of protein degradation pathways, mitochondrial damage, and oxidative stress) (Blesa et al., 2015; Tysnes and Storstein, 2017).

PD treatment is predominantly focused on the dopaminergic pathway, although alternative approaches such as deep brain stimulation (DBS) are suitable for later-stage disease. The most important drug for the treatment of PD is L-dopa; when passing through the cranioencephalic barrier, it

converts dopamine into the remaining dopaminergic neurons of the black substance, dopamine agonists, which directly stimulate the D1–3 receptors in the striatum without the requirement for further metabolism within the dopaminergic neurons. Monoamine oxidase B (MAO-B) inhibitors and safinamide rely on decreasing dopamine metabolism and prolong and potentiate dopaminergic stimulation.

Safinamide is a new option for treating PD, which acts as a reversible inhibitor of MAO-B, with additional properties including blockade of voltage-dependent sodium channels, modulating calcium channels, and inhibiting glutamate release. Catechol-*O*-methyl transferase inhibitors, anticholinergic drugs, amantadine, and serotonin are also used. Other therapies are deep brain stimulation to the subthalamic nucleus, which stimulates the activity of neurons. There are also treatments of natural origin which not only are palliative but also do not stop neurodegeneration (Oertel and Schulz, 2016; Rizek et al., 2016; Seppi et al., 2019). Scientists have tried to find new treatments that help improve patients' quality of life; in these investigations, it was found that phytochemical compounds (resveratrol, curcumin, berberine, and celastrol, among others) have neuroprotective activity against the dopaminergic system, thus inhibiting cell apoptosis. Also, nanoscale delivery systems have been investigated because most components can lose their effectiveness before reaching the required site. This type of system is a good reservoir to carry drugs where they are needed (Javed et al., 2019; Kuo and Rajesh, 2018; Shahpiri et al., 2016;Yoosefian et al., 2018).

2.3.1.6 Osteoarthritis

Osteoarthritis is one of the most prevalent chronic degenerative diseases. It occurs mainly in women. The main risk factors are age, obesity, lack of physical activity, chronic stress, and a poor diet (Dobson et al., 2018; Malfait, 2016). It is characterized by inflammation in the joints. Other reported symptoms are pain (it can be presented in two different ways: intermittent or constant), joint swelling, clicking, locking, cramping, reduced range of motion, and deformity. It has been found that this inflammation occurs mainly in the hip, knee, and proximal interphalangeal joints. In almost all patients, it has been found that there is an accumulation of synovial fluid, bone deformation, and activation of the inflammation signal cascade. X-rays can help determine treatment clearly (Abramoff and Caldera, 2020; Glyn-Jones et al., 2015). Treatments can be pharmacological and nonpharmacological, where the latter is related to increasing the patient's physical activity as well as losing weight.

On the other hand, pharmacological treatment involves both the intake and the topical use of nonsteroidal anti-inflammatory drugs (diclofenac), intra-articular drugs (corticosteroids), and hyaluronic acid. Alternative treatments such as acupuncture, laser, and electromagnetic therapy are also available, but the information is still unclear. When the disease is already very severe, it is best to perform surgery (Jones et al., 2019; Nelson, 2018). Because the disease is triggered by the lack of control of the inflammation process, new alternatives have been sought to help control this process, including serotonin-norepinephrine reuptake inhibitors which would help reduce pain in patients. Strontium ranelate inhibits subchondral bone resorption by regulating the activity of osteoprotegerin, RANK ligand and matrix metalloproteinases, and IL-1 receptor antagonists, which stimulates the production of metalloproteases while reducing the production of aggrecan. This is involved in the driving factor in the degenerative process occurring in the osteoarthritis joint and proteoglycan and also antibodies to the nerve growth factor (NGF) because they play a very important role in pain and the central nervous system. Finally, regenerative therapy uses stem cells to transform tissues into different types (Wang et al., 2015; Whitney et al., 2017; Wu et al., 2018).

Another alternative would be to eat a diet rich in the different phytochemical compounds (polyphenols, antioxidants) because these are effective against some cytokines (e.g., IL-8) secreted during the process. In addition, the use of different compounds such as alginate, chitosan, and polymeric nanoparticles helps regenerate damaged cartilages or release a specific drug or gene (Bhattacharya et al., 2020; Eichaker et al., 2014; Geiger et al., 2018; Herrero-Beaumont et al., 2017; Maudens et al., 2018; Mohammadinejad et al., 2020).

2.3.1.7 Chronic kidney diseases

Chronic kidney disease is caused mainly by diabetes and hypertension. It occurs in a greater proportion of adults >55 years of age. There are also socioeconomic factors that influence its appearance, such as obesity, smoking, and drinking excessively, among others (Ammirati, 2020; Nicholas et al., 2015). Chronic kidney disease is characterized by damage as either functional abnormalities of the kidneys (such as proteinuria or albuminuria or abnormalities of the urinary sediment, such as dysmorphic red cells) or structural abnormalities as noted on imaging studies. Different analyses are recommended to diagnose kidney damage, for example, glomerular filtration rate, renal ultrasound, urinalysis

with albumin–creatinine ratio/protein–creatinine ratio, renal biopsy, serum immunology, and myeloma screen in urine (Findlay and Isles, 2015; Romagnani et al., 2017). The symptoms presented by patients in the early stages of the disease do not normally manifest, so the disease is mainly associated with hypertension and diabetes. Patients who do not have proper diabetes treatment may present nephrotic diabetes if they present proteinuria in the same way for patients who suffer from hypertension (Drawz and Rahman, 2015). Within the nonpharmacological treatments, changing the diet (a diet high in fruits, vegetables, and grains) and the lifestyle is very effective, for example, not smoking, exercising 30 min a day, not drinking alcohol, and maintaining the body mass index within the normal limit (Romagnani et al., 2017). If it is not treated in time, this can complicate anemia, bone disease, hyperkalemia, acidosis, and malnutrition (Del Vecchio and Locatelli, 2018; Findlay and Isles, 2015). In very rare cases, neurological complications may occur derived from the activation of processes such as oxidative stress, inflammation, calcification of the vascular wall, endothelial dysfunction, and the accumulation of uremic toxins, which is why other alternatives have been sought to prevent patients from getting these types of complications. For example, the use of phytochemicals (tannins, flavonoids, alkaloids, phenols, etc.) present in medicinal plants and the combination of both conventional and herbal treatments (curcumin, turmeric, olive, green tea, resveratrol, etc.) can also help the patient to mitigate some diseases derived from CKD (Chillon et al., 2016; Kpemissi et al., 2019; Shah et al., 2017).

2.3.2 Socioeconomic impact

According to the World Health Organization (2010), in high-income countries, only 13% of the deaths related to NCDs occur under the age of 60, whereas in low-income countries, this number is close to 60%. This is mainly because of a difference between the health systems that goes hand in hand with the development of the countries (Durrani, 2016). Because of the economic problems that developing countries face, the increase in noncommunicable diseases makes their correct management very complex. Also, NCDs have large financial consequences, and because they are chronic, they require long-lasting and expensive specialized treatment (Subramanian et al., 2018).

This rapidly growing burden of NCDs in developing countries is because of urbanization and the introduction of an increasingly sedentary life because of globalization (Bhattacharya et al., 2020). One of the main problems in these countries is that the purchasing power of the inhabitants

is low, forcing them to consume affordable food, better known as fast food, which is high in fat, sugar, and salt. Besides, these people find comfort in activities such as alcoholism and smoking. All this, far from promoting a better life, leads them to have a high probability of suffering from noncommunicable diseases and, in that case, dying from them (Islam et al., 2014).

On the other hand, medical care is of higher quality in developed countries. In addition, there is more purchasing power for a correct diet and the ability to carry out nonharmful recreational activities. Because of the above, people in a socially disadvantaged situation die sooner than people of a higher social situation (Williams et al., 2018).

NCDs contribute to social inequities as they have been categorized as a major risk to economic loss; they are now compared to economic risks such as fiscal crises, unemployment, and underinvestment in infrastructure (Jaspers et al., 2015). The major NCDs promoting socioeconomical problems are coronary heart disease, stroke, cancer (lung, colon, cervical, and breast), chronic obstructive pulmonary disease, diabetes mellitus, and chronic kidney disease. A meta-analysis revealed that cancer and CVD had the highest mean annual direct costs, with an estimated 197,772 and 81,096 USD per patient, respectively. As for indirect costs, diabetes and cancer are the leading NCDs with annual mean costs of 24,740 and 23,418 USD per patient, respectively (Muka et al., 2015).

As for diabetes, a low household income and a low educational level are associated with the prevalence of this disease in patients older than 30 years (Suwannaphant et al., 2017). On the other hand, people with a higher education level and higher income are less likely to develop diabetes in their lifetime (Kim et al., 2015b). It is estimated that the direct cost associated with diabetes will increase from 1.3 trillion dollars worldwide, which was estimated in 2015, to 2.1 trillion dollars by 2030 (Bommer et al., 2018).

As for cancer, the last report of the World Health Organization (2010) announced a total annual cost of 1.16 trillion dollars. Regarding dementia, the total cost worldwide was estimated as 818 US billion dollars in 2105, but it was estimated that it could reach 2 trillion dollars by 2030 (El-Hayek et al., 2019).

Research to date, largely drawn from high-income countries, suggests that disadvantaged and marginalized groups have a higher NCD burden. However, there has been a shortage of research studying this relationship within low- and lower-middle-income countries. A recent review found a significant association between cancer and socioeconomic status, suggesting that groups with a low socioeconomic status had a higher risk of developing

cancer. In the same way, they found a significant relationship between the development of CVDs and the groups with a low socioeconomic status. On the contrary, for diabetes, they found a significant relationship with the groups with a higher socioeconomic level, which had a higher risk of developing diabetes. They did not find significant findings in chronic respiratory diseases (Williams et al., 2018).

2.4 Conclusions and perspectives

Noncommunicable diseases are inclined to be long-lasting and result from a combination of genetic, physiological, environmental, and behavioral factors. The most important metabolic risk factors could be considered: increased blood pressure, obesity, hyperglycemia, and hyperlipidemia. The most important strategy to reduce the incidence of NCDs is changing lifestyle, stopping smoking, and reducing overweight and obesity. The above will represent great improvements to human health. Otherwise, the socioeconomic factor is closely related to the development of these diseases because generally vulnerable and socially disadvantaged people get sicker and die earlier than those with a higher social position because they run a greater risk of exposure to harmful products, such as tobacco, or unhealthy eating practices, in addition to limited access to health services. Because of this, improvement in the detection, screening, and treatment of these diseases is of utmost importance. High-impact essential interventions against these diseases can be carried out in primary care to reinforce early detection and early treatment. However, further research is needed regarding the association between NCDs and socioeconomic status, especially in low-income and lower-middle-income countries. In order to achieve this goal, initially, a measure of the socioeconomic status must be unified and correlate with other established WHO measures. If this is achieved, it would be possible to establish more robust and conclusive relationships between NCDs and the socioeconomic status. Undoubtedly, another important thing is to develop a comprehensive approach that makes all sectors, including health, economics, education, agriculture, and planning, collaborate to reduce their risks.

References

Abramoff, B., Caldera, F.E., 2020. Osteoarthritis: pathology, diagnosis, and treatment options. Med. Clin. North Am. 104 (2), 293–311. https://doi.org/10.1016/j.mcna.2019.10.007.

Agha, M., Agha, R., 2017. The rising prevalence of obesity: part A: impact on public health. Int. J. Surg. Oncol. 2 (7), e17.

Agustí, A., Edwards, L.D., Rennard, S.I., MacNee, W., Tal-Singer, R., Miller, B.E., et al., 2012. Persistent systemic inflammation is associated with poor clinical outcomes in COPD: a novel phenotype. PLoS One 7 (5). https://doi.org/10.1371/journal.pone.0037483, e37483.

Akselrod, S., Bloomfield, A., Marmot, M., Moran, A.E., Nishtar, S., Placella, E., 2019. Mobilising Society to Implement Solutions for Noncommunicable Diseases. British Medical Journal Publishing Group.

Albarracin, S.L., Stab, B., Casas, Z., Sutachan, J.J., Samudio, I., Gonzalez, J., et al., 2012. Effects of natural antioxidants in neurodegenerative disease. Nutr. Neurosci. 15 (1), 1–9. https://doi.org/10.1179/1476830511Y.0000000028.

Alkabban, F.M., Ferguson, T., 2019. Cancer, breast. In: StatPearls [Internet]. StatPearls Publishing.

Al-Sajee, D., Oliveria, J.P., Sehmi, R., Gauvreau, G.M., 2018. Antialarmins for treatment of asthma: future perspectives. Curr. Opin. Pulm. Med. 24 (1), 32–41. https://doi.org/10.1097/mcp.0000000000000443.

Alzheimer's, A., 2019. 2019 Alzheimer's disease facts and figures. Alzheimers Dement. 15 (3), 321–387. https://doi.org/10.1016/j.jalz.2019.01.010.

Amelink, M., de Groot, J.C., de Nijs, S.B., Lutter, R., Zwinderman, A.H., Sterk, P.J., et al., 2013. Severe adult-onset asthma: a distinct phenotype. J. Allergy Clin. Immunol. 132 (2), 336–341. https://doi.org/10.1016/j.jaci.2013.04.052.

Ammirati, A.L., 2020. Chronic kidney disease. Rev. Assoc. Med. Bras. 66, s03–s09. Retrieved from http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-42302020001300003&nrm=iso.

Angrini, M., Varthaman, A., Garcia-Verdugo, I., Sallenave, J.-M., Alifano, M., Cremer, I., 2021. To vaccinate or not: influenza virus and lung cancer progression. Trends Cancer. https://doi.org/10.1016/j.trecan.2021.02.006.

Armstrong, M.J., Okun, M.S., 2020. Diagnosis and treatment of Parkinson disease: a review. JAMA 323, 548–560. 1538-3598 (Electronic).

Arnett, D.K., Blumenthal, R.S., Albert, M.A., Buroker, A.B., Goldberger, Z.D., Hahn, E.J., et al., 2019. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 140 (11), e596–e646. https://doi.org/10.1161/CIR.0000000000000678.

Asai, N., Ohkuni, Y., Kaneko, N., Yamaguchi, E., Kubo, A., 2014. Relapsed small cell lung cancer: treatment options and latest developments. Ther. Adv. Med. Oncol. 6 (2), 69–82.

Atkinson, M.A., Eisenbarth, G.S., Michels, A.W., 2014. Type 1 diabetes. Lancet 383 (9911), 69–82. https://doi.org/10.1016/S0140-6736(13)60591-7.

Avgerinos, K.I., Spyrou, N., Mantzoros, C.S., Dalamaga, M., 2019. Obesity and cancer risk: emerging biological mechanisms and perspectives. Metab. Clin. Exp. 92, 121–135. https://doi.org/10.1016/j.metabol.2018.11.001.

Baek, S.K., Lee, K.T., Bae, S.B., Lee, S.-C., 2019. Evaluating the recent developments in palliative chemotherapy for metastatic colorectal cancer. Korean J. Intern. Med. 34 (6), 1188.

Baldi, S., Dellacà, R., Govoni, L., Torchio, R., Aliverti, A., Pompilio, P., et al., 2010. Airway distensibility and volume recruitment with lung inflation in COPD. J. Appl. Physiol. (1985) 109 (4), 1019–1026. https://doi.org/10.1152/japplphysiol.00147.2010.

Balestrino, R., Schapira, A.H.V., 2020. Parkinson disease. Eur. J. Neurol. 27 (1), 27–42. https://doi.org/10.1111/ene.14108.

Bantz, S.K., Zhu, Z., Zheng, T., 2014. The atopic march: progression from atopic dermatitis to allergic rhinitis and asthma. J. Clin. Cell. Immunol. 5 (2), 202. https://doi.org/10.4172/2155-9899.1000202.

Bekris, L.M., Yu, C.-E., Bird, T.D., Tsuang, D., 2011. The genetics of Alzheimer's disease and Parkinson's disease. In: Blass, J.P. (Ed.), Neurochemical Mechanisms in Disease. Springer New York, New York, NY, pp. 695–755.

Belsky, D.W., Sears, M.R., 2014. The potential to predict the course of childhood asthma. Expert Rev. Respir. Med. 8 (2), 137–141. https://doi.org/10.1586/17476348.2014.879826.
Bertram, L., Tanzi, R.E., 2012. The genetics of Alzheimer's disease. Prog. Mol. Biol. Transl. Sci. 107, 79–100. 1878-0814 (Electronic).
Bhattacharya, S., Mandal, S.K., Akhtar, M.S., Dastider, D., Sarkar, S., Bose, S., et al., 2020. Phytochemicals in the treatment of arthritis: current knowledge. Int. J. Curr. Pharm. Res. 12 (4), 1–6. https://doi.org/10.22159/ijcpr.2020v12i4.39050.
Billington, C.K., Penn, R.B., Hall, I.P., 2017. β(2) agonists. Handb. Exp. Pharmacol. 237, 23–40. https://doi.org/10.1007/164_2016_64.
Blackadar, C.B., 2016. Historical review of the causes of cancer. World J. Clin. Oncol. 7 (1), 54.
Blesa, J., Trigo-Damas, I., Quiroga-Varela, A., Jackson-Lewis, V.R., 2015. Oxidative stress and Parkinson's disease. Front. Neuroanat. *9*, 91. https://doi.org/10.3389/fnana.2015.00091.
Board, P.C.G.E., 2019. Genetics of colorectal cancer (PDQ®). In: PDQ Cancer Information Summaries [Internet]. National Cancer Institute (US).
Bolós, M., Perea, J.R., Avila, J., 2017. Alzheimer's disease as an inflammatory disease. Biomol. Concepts 8 (1), 37–43. https://doi.org/10.1515/bmc-2016-0029.
Bommer, C., Sagalova, V., Heesemann, E., Manne-Goehler, J., Atun, R., Bärnighausen, T., et al., 2018. Global economic burden of diabetes in adults: projections from 2015 to 2030. Diabetes Care 41 (5), 963–970.
Bondi, M.W., Edmonds, E.C., Salmon, D.P., 2017. Alzheimer's disease: past, present, and future. J. Int. Neuropsychol. Soc. 23, 818–831. https://doi.org/10.1017/S135561771700100X. 1469-7661 (Electronic).
Boura-Halfon, S., Zick, Y., 2009. Phosphorylation of IRS proteins, insulin action, and insulin resistance. Am. J. Physiol. Endocrinol. Metab. 296 (4), E581–E591. https://doi.org/10.1152/ajpendo.90437.2008.
Brenner, H., Rothenbacher, D., Arndt, V., 2009. Epidemiology of stomach cancer. Cancer Epidemiol., 467–477.
Brown Rebecca, C., Lockwood Alan, H., Sonawane Babasaheb, R., 2005. Neurodegenerative diseases: an overview of environmental risk factors. Environ. Health Perspect. 113 (9), 1250–1256. https://doi.org/10.1289/ehp.7567.
Budreviciute, A., Damiati, S., Sabir, D.K., Onder, K., Schuller-Goetzburg, P., Plakys, G., et al., 2020. Management and prevention strategies for noncommunicable diseases (NCDs) and their risk factors. Front. Public Health 8, 788.
Butler, M., McCreedy, E., Nelson, V.A., Desai, P., Ratner, E., Fink, H.A., et al., 2017. Does cognitive training prevent cognitive decline? Ann. Intern. Med. 168 (1), 63–68. https://doi.org/10.7326/M17-1531.
Centers for Disease Control and Prevention, 2021. Types of stroke. Retrieved from https://www.cdc.gov/stroke/types_of_stroke.htm.
Chen, Z., Zhong, C., 2014. Oxidative stress in Alzheimer's disease. Neurosci. Bull. 30 (2), 271–281. https://doi.org/10.1007/s12264-013-1423-y.
Chen, X., Liu, H.-P., Li, M., Qiao, L., 2014. Advances in non-surgical management of primary liver cancer. World J. Gastroenterol. 20 (44), 16630.
Chen, R., Gan, Y., Ge, N., Chen, Y., Wang, Y., Zhang, B., et al., 2016. Transarterial chemoembolization versus radiofrequency ablation for recurrent hepatocellular carcinoma after resection within Barcelona clinic liver cancer stage 0/a: a retrospective comparative study. J. Vasc. Interv. Radiol. 27 (12), 1829–1836.
Chen, M.-K., Mecca, A.P., Naganawa, M., Finnema, S.J., Toyonaga, T., Lin, S.-F., et al., 2018. Assessing synaptic density in Alzheimer disease with synaptic vesicle glycoprotein 2A positron emission tomographic imaging. JAMA Neurol. 75 (10), 1215–1224. https://doi.org/10.1001/jamaneurol.2018.1836.

Chen, D., Wu, J., Jin, D., Wang, B., Cao, H., 2019. Fecal microbiota transplantation in cancer management: current status and perspectives. Int. J. Cancer 145 (8), 2021–2031. https://doi.org/10.1002/ijc.32003.

Chillon, J.-M., Massy, Z.A., Stengel, B., 2016. Neurological complications in chronic kidney disease patients. Nephrol. Dial. Transplant. 31 (10), 1606–1614. https://doi.org/10.1093/ndt/gfv315.

Conget, I., 2002. Diagnóstico, clasificación y patogenia de la diabetes mellitus. Rev. Esp. Cardiol. 55 (5), 528–538. Retrieved from https://www.revespcardiol.org/es-diagnostico-clasificacion-patogenia-diabetes-mellitus-articulo-13031154.

Coulthard, E.J., Love, S., 2018. A broader view of dementia: multiple co-pathologies are the norm. Brain 141 (7), 1894–1897. https://doi.org/10.1093/brain/awy153.

Custovic, A., 2015. To what extent is allergen exposure a risk factor for the development of allergic disease? Clin. Exp. Allergy 45 (1), 54–62. https://doi.org/10.1111/cea.12450.

Dahm, C.C., Keogh, R.H., Spencer, E.A., Greenwood, D.C., Key, T.J., Fentiman, I.S., et al., 2010. Dietary fiber and colorectal cancer risk: a nested case–control study using food diaries. J. Natl. Cancer Inst. 102 (9), 614–626.

Daly, B., Toulis, K.A., Thomas, N., Gokhale, K., Martin, J., Webber, J., et al., 2018. Increased risk of ischemic heart disease, hypertension, and type 2 diabetes in women with previous gestational diabetes mellitus, a target group in general practice for preventive interventions: a population-based cohort study. PLoS Med. 15 (1). https://doi.org/10.1371/journal.pmed.1002488.

Del Vecchio, L., Locatelli, F., 2018. Roxadustat in the treatment of anaemia in chronic kidney disease. Expert Opin. Investig. Drugs 27 (1), 125–133. https://doi.org/10.1080/13543784.2018.1417386.

DeMichele-Sweet, M.A., Sweet, R.A., 2010. Genetics of psychosis in Alzheimer's disease: a review. J. Alzheimers Dis. 19 (3), 761–780. https://doi.org/10.3233/JAD-2010-1274.

DeTure, M.A., Dickson, D.W., 2019. The neuropathological diagnosis of Alzheimer's disease. Mol. Neurodegener. 14 (1), 32. https://doi.org/10.1186/s13024-019-0333-5.

Dickson, D.W., 2018. Neuropathology of Parkinson's disease. Parkinsonism Relat. Disord. 46, S30–S33. https://doi.org/10.1016/j.parkreldis.2017.07.033.

Divella, R., De Luca, R., Abbate, I., Naglieri, E., Daniele, A., 2016. Obesity and cancer: the role of adipose tissue and adipocytokines-induced chronic inflammation. J. Cancer 7 (15), 2346–2359. https://doi.org/10.7150/jca.16884.

Divo, M., Cote, C., de Torres, J.P., Casanova, C., Marin, J.M., Pinto-Plata, V., et al., 2012. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. 186 (2), 155–161. https://doi.org/10.1164/rccm.201201-0034OC.

Dobson, G.P., Letson, H.L., Grant, A., McEwen, P., Hazratwala, K., Wilkinson, M., Morris, J.L., 2018. Defining the osteoarthritis patient: back to the future. Osteoarthr. Cartil. 26 (8), 1003–1007. https://doi.org/10.1016/j.joca.2018.04.018.

Drawz, P., Rahman, M., 2015. Chronic kidney disease. Ann. Intern. Med. 162 (11), ITC1–ITC16. https://doi.org/10.7326/AITC201506020.

Drazner, M.H., 2011. The progression of hypertensive heart disease. Circulation 123 (3), 327–334. https://doi.org/10.1161/CIRCULATIONAHA.108.845792.

Durrani, H., 2016. Healthcare and healthcare systems: inspiring progress and future prospects. mHealth 2.

Eichaker, L.R., Cho, H., Duvall, C.L., Werfel, T.A., Hasty, K.A., 2014. Future nanomedicine for the diagnosis and treatment of osteoarthritis. Nanomedicine 9 (14), 2203–2215. https://doi.org/10.2217/nnm.14.138.

El-Hayek, Y.H., Wiley, R.E., Khoury, C.P., Daya, R.P., Ballard, C., Evans, A.R., et al., 2019. Tip of the iceberg: assessing the global socioeconomic costs of Alzheimer's disease and related dementias and strategic implications for stakeholders. J. Alzheimers Dis. 70 (2), 323–341.

Evert, A.B., Boucher, J.L., Cypress, M., Dunbar, S.A., Franz, M.J., Mayer-Davis, E.J., et al., 2013. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care 36 (11), 3821–3842. https://doi.org/10.2337/dc13-2042.

Findlay, M., Isles, C., 2015. Overview of chronic kidney disease. In: Findlay, M., Isles, C. (Eds.), Clinical Companion in Nephrology. Springer International Publishing, Cham, pp. 101–106.

Fu, L., Freishtat, R.J., Gordish-Dressman, H., Teach, S.J., Resca, L., Hoffman, E.P., Wang, Z., 2014. Natural progression of childhood asthma symptoms and strong influence of sex and puberty. Ann. Am. Thorac. Soc. 11 (6), 939–944. https://doi.org/10.1513/AnnalsATS.201402-084OC.

Gandhi, G.R., Vasconcelos, A.B.S., Haran, G.H., Calisto, V.K.d.S., Jothi, G., Quintans, J.d.S.S., et al., 2020. Essential oils and its bioactive compounds modulating cytokines: a systematic review on anti-asthmatic and immunomodulatory properties. Phytomedicine 73. https://doi.org/10.1016/j.phymed.2019.152854, 152854.

GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 392 (10159), 1789–1858.

Geiger, B.C., Wang, S., Padera, R.F., Grodzinsky, A.J., Hammond, P.T., 2018. Cartilage-penetrating nanocarriers improve delivery and efficacy of growth factor treatment of osteoarthritis. Sci. Transl. Med. 10 (469). https://doi.org/10.1126/scitranslmed.aat8800, eaat8800.

Gelband, H., Sloan, F.A., 2007. Cancer Control Opportunities in Low- and Middle-Income Countries. National Academies Press (US), Washington, DC.

Giacoppo, S., Galuppo, M., Montaut, S., Iori, R., Rollin, P., Bramanti, P., Mazzon, E., 2015. An overview on neuroprotective effects of isothiocyanates for the treatment of neurodegenerative diseases. Fitoterapia 106, 12–21. https://doi.org/10.1016/j.fitote.2015.08.001.

Glyn-Jones, S., Palmer, A.J.R., Agricola, R., Price, A.J., Vincent, T.L., Weinans, H., Carr, A.J., 2015. Osteoarthritis. Lancet 386 (9991), 376–387. https://doi.org/10.1016/S0140-6736(14)60802-3.

Godyń, J., Jończyk, J., Panek, D., Malawska, B., 2016. Therapeutic strategies for Alzheimer's disease in clinical trials. Pharmacol. Rep. 68 (1), 127–138. https://doi.org/10.1016/j.pharep.2015.07.006.

Gowshall, M., Taylor-Robinson, S.D., 2018. The increasing prevalence of non-communicable diseases in low-middle income countries: the view from Malawi. Int. J. Gen. Med. 11, 255.

Gupta, G.K., Collier, A.L., 2020. Perspectives on triple-negative breast cancer: current treatment strategies, unmet needs, and potential targets for future therapies. Cancers (Basel) 12 (9). https://doi.org/10.3390/cancers12092392.

Haggar, F.A., Boushey, R.P., 2009. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clin. Colon Rectal Surg. 22 (4), 191.

Hamaguchi, T., Ono, K., Yamada, M., 2010. Review: curcumin and Alzheimer's disease. CNS Neurosci. Ther. 16, 285–297. 1755-5949 (Electronic).

Heffler, E., Blasi, F., Latorre, M., Menzella, F., Paggiaro, P., Pelaia, G., et al., 2019. The severe asthma network in Italy: findings and perspectives. J. Allergy Clin. Immunol. Pract. 7 (5), 1462–1468. https://doi.org/10.1016/j.jaip.2018.10.016.

Hemphill, J.C., Greenberg, S.M., Anderson, C.S., Becker, K., Bendok, B.R., Cushman, M., et al., 2015. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 46 (7), 2032–2060. https://doi.org/10.1161/STR.0000000000000069.

Heneka, M.T., Carson, M.J., Khoury, J.E., Landreth, G.E., Brosseron, F., Feinstein, D.L., et al., 2015. Neuroinflammation in Alzheimer's disease. Lancet Neurol. 14 (4), 388–405. https://doi.org/10.1016/S1474-4422(15)70016-5.

Herrero-Beaumont, G., Roman-Blas, J.A., Bruyère, O., Cooper, C., Kanis, J., Maggi, S., et al., 2017. Clinical settings in knee osteoarthritis: pathophysiology guides treatment. Maturitas 96, 54–57. https://doi.org/10.1016/j.maturitas.2016.11.013.

Hider, R.C., Roy, S., Ma, Y.M., Le Kong, X., Preston, J., 2011. The potential application of iron chelators for the treatment of neurodegenerative diseases. Metallomics 3, 239–249. 1756-591X (Electronic).

Holgate, S.T., Wenzel, S., Postma, D.S., Weiss, S.T., Renz, H., Sly, P.D., 2015. Asthma. Nat. Rev. Dis. Primers. 1 (1). https://doi.org/10.1038/nrdp.2015.25, 15025.

Hou, Y., Dan, X., Babbar, M., Wei, Y., Hasselbalch, S.G., Croteau, D.L., Bohr, V.A., 2019. Ageing as a risk factor for neurodegenerative disease. Nat. Rev. Neurol. 15 (10), 565–581. https://doi.org/10.1038/s41582-019-0244-7.

Hu, J., La Vecchia, C., Negri, E., de Groh, M., Morrison, H., Mery, L., 2015. Macronutrient intake and stomach cancer. Cancer Causes Control 26 (6), 839–847.

International Agency for Research on Cancer, 2020. Cancer today. Retrieved on August 12, 2021 from https://gco.iarc.fr/today/home.

Iqbal, J., Ginsburg, O., Rochon, P.A., Sun, P., Narod, S.A., 2015. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States. JAMA 313 (2), 165–173.

Islam, S.M.S., Purnat, T.D., Phuong, N.T.A., Mwingira, U., Schacht, K., Fröschl, G., 2014. Non-communicable diseases (NCDs) in developing countries: a symposium report. Global. Health 10 (1), 1–8.

Jaspers, L., Colpani, V., Chaker, L., van der Lee, S.J., Muka, T., Imo, D., et al., 2015. The global impact of non-communicable diseases on households and impoverishment: a systematic review. Eur. J. Epidemiol. 30 (3), 163–188.

Javed, H., Nagoor Meeran, M.F., Azimullah, S., Adem, A., Sadek, B., Ojha, S.K., 2019. Plant extracts and phytochemicals targeting α-synuclein aggregation in Parkinson's disease models. Front. Pharmacol. 9, 1555. https://doi.org/10.3389/fphar.2018.01555.

Jiang, T., Dai, L., Li, P., Zhao, J., Wang, X., An, L., et al., 2021. Lipid metabolism and identification of biomarkers in asthma by lipidomic analysis. Biochim. Biophys. Acta Mol. Cell Biol. Lipids 1866 (2). https://doi.org/10.1016/j.bbalip.2020.158853, 158853.

Johnson, C.M., Wei, C., Ensor, J.E., Smolenski, D.J., Amos, C.I., Levin, B., Berry, D.A., 2013. Meta-analyses of colorectal cancer risk factors. Cancer Causes Control 24 (6), 1207–1222.

Jones, I.A., Togashi, R., Wilson, M.L., Heckmann, N., Vangsness, C.T., 2019. Intra-articular treatment options for knee osteoarthritis. Nat. Rev. Rheumatol. 15 (2), 77–90. https://doi.org/10.1038/s41584-018-0123-4.

Kalemkerian, G.P., Akerley, W., Bogner, P., Borghaei, H., Chow, L.Q., Downey, R.J., et al., 2013. Small cell lung cancer. J. Natl. Compr. Canc. Netw. 11 (1), 78–98.

Keymeulen, B., Vandemeulebroucke, E., Ziegler, A.G., Mathieu, C., Kaufman, L., Hale, G., et al., 2005. Insulin needs after CD3-antibody therapy in new-onset type 1 diabetes. N. Engl. J. Med. 352 (25), 2598–2608. https://doi.org/10.1056/NEJMoa043980.

Kim, G.H., Kim, J.E., Rhie, S.J., Yoon, S., 2015a. The role of oxidative stress in neurodegenerative diseases. Exp. Neurobiol. 24 (4), 325–340. https://doi.org/10.5607/en.2015.24.4.325.

Kim, Y.J., Jeon, J.Y., Han, S.J., Kim, H.J., Lee, K.W., Kim, D.J., 2015b. Effect of socioeconomic status on the prevalence of diabetes. Yonsei Med. J. 56 (3), 641.

Kim, H.-I., Lim, H., Moon, A., 2018. Sex differences in cancer: epidemiology, genetics and therapy. Biomol. Ther. 26 (4), 335.

Kizilay, F., Gali, H.E., Serefoglu, E.C., 2017. Diabetes and sexuality. Sex. Med. Rev. 5 (1), 45–51. https://doi.org/10.1016/j.sxmr.2016.07.002.

Kovacs, G.G., 2017. Concepts and classification of neurodegenerative diseases. Handb. Clin. Neurol. 145, 301–307. https://doi.org/10.1016/B978-0-12-802395-2.00021-3.

Kovacs, G.G., 2018. Chapter 21—Concepts and classification of neurodegenerative diseases. In: Kovacs, G.G., Alafuzoff, I. (Eds.), Handbook of Clinical Neurology. vol. 145. Elsevier, pp. 301–307.

Kpemissi, M., Eklu-Gadegbeku, K., Veerapur, V.P., Potârniche, A.-V., Adi, K., Vijayakumar, S., et al., 2019. Antioxidant and nephroprotection activities of *Combretum micranthum*: a phytochemical, in-vitro and ex-vivo studies. Heliyon 5 (3). https://doi.org/10.1016/j.heliyon.2019.e01365.

Kumar, A., Singh, A., Ekavali, 2015. A review on Alzheimer's disease pathophysiology and its management: an update. Pharmacol. Rep. 67 (2), 195–203. https://doi.org/10.1016/j.pharep.2014.09.004.

Kuo, Y.-C., Rajesh, R., 2018. Current development of nanocarrier delivery systems for Parkinson's disease pharmacotherapy. J. Taiwan Inst. Chem. Eng. 87, 15–25. https://doi.org/10.1016/j.jtice.2018.03.028.

Laws, K.R., Irvine, K., Gale, T.M., 2018. Sex differences in Alzheimer's disease. Curr. Opin. Psychiatry *32*, 133–139. 1473-6578 (Electronic).

Lemjabbar-Alaoui, H., Hassan, O.U., Yang, Y.-W., Buchanan, P., 2015. Lung cancer: biology and treatment options. Biochim. Biophys. Acta Rev. Cancer 1856 (2), 189–210.

Lisy, K., Aromataris, E., Moola, S., Tufanaru, C., Lockwood, C., 2016. Magnitude and scope of non-communicable disease-related disability: a systematic review protocol. JBI Database System Rev. Implement. Rep. 14 (10), 112–133.

Maher, P., 2019. The potential of flavonoids for the treatment of neurodegenerative diseases. Int. J. Mol. Sci. 20 (12), 3056. https://doi.org/10.3390/ijms20123056.

Maiti, P., Dunbar, G.L., 2018. Use of curcumin, a natural polyphenol for targeting molecular pathways in treating age-related neurodegenerative diseases. Int. J. Mol. Sci. 19 (6), 1637. https://doi.org/10.3390/ijms19061637.

Malfait, A.M., 2016. Osteoarthritis year in review 2015: biology. Osteoarthr. Cartil. 24 (1), 21–26. https://doi.org/10.1016/j.joca.2015.09.010.

Malta, D.C., Franca, E., Abreu, D.M.X., Perillo, R.D., Salmen, M.C., Teixeira, R.A., et al., 2017. Mortality due to noncommunicable diseases in Brazil, 1990 to 2015, according to estimates from the Global Burden of Disease study. Sao Paulo Med. J. 135 (3), 213–221.

Mathyssen, C., Gayan-Ramirez, G., Bouillon, R., Janssens, W., 2017. Vitamin D supplementation in respiratory diseases: evidence from randomized controlled trials. Pol. Arch. Intern. Med. 127 (11), 775–784. https://doi.org/10.20452/pamw.4134.

Matsuda, M., Tsuruta, M., Hasegawa, H., Okabayashi, K., Kondo, T., Shimada, T., et al., 2016. Transanal drainage tube placement to prevent anastomotic leakage following colorectal cancer surgery with double stapling reconstruction. Surg. Today 46 (5), 613–620.

Maudens, P., Seemayer, C.A., Thauvin, C., Gabay, C., Jordan, O., Allémann, E., 2018. Nanocrystal–polymer particles: extended delivery carriers for osteoarthritis treatment. Small 14 (8). https://doi.org/10.1002/smll.201703108, 1703108.

Modi, G., Pillay, V., Choonara, Y.E., 2010. Advances in the treatment of neurodegenerative disorders employing nanotechnology. Ann. N.Y. Acad. Sci. 1184, 154–172.

Mohammadinejad, R., Ashrafizadeh, M., Pardakhty, A., Uzieliene, I., Denkovskij, J., Bernotiene, E., et al., 2020. Nanotechnological strategies for osteoarthritis diagnosis, monitoring, clinical management, and regenerative medicine: recent advances and future opportunities. Curr. Rheumatol. Rep. 22 (4), 12. https://doi.org/10.1007/s11926-020-0884-z.

Moin, A.S.M., Nandakumar, M., Diane, A., Dehbi, M., Butler, A.E., 2021. The role of heat shock proteins in type 1 diabetes. Front. Immunol. 11 (3459). https://doi.org/10.3389/fimmu.2020.612584.

Moore, W.C., Meyers, D.A., Wenzel, S.E., Teague, W.G., Li, H., Li, X., et al., 2010. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. Am. J. Respir. Crit. Care Med. 181 (4), 315–323. https://doi.org/10.1164/rccm.200906-0896OC.

Morse, D., Rosas, I.O., 2014. Tobacco smoke–induced lung fibrosis and emphysema. Annu. Rev. Physiol. 76 (1), 493–513. https://doi.org/10.1146/annurev-physiol-021113-170411.
Muka, T., Imo, D., Jaspers, L., Colpani, V., Chaker, L., van der Lee, S.J., et al., 2015. The global impact of non-communicable diseases on healthcare spending and national income: a systematic review. Eur. J. Epidemiol. 30 (4), 251–277.
Murea, M., Ma, L., Freedman, B.I., 2012. Genetic and environmental factors associated with type 2 diabetes and diabetic vascular complications. Rev. Diabet. Stud. 9 (1), 6–22. https://doi.org/10.1900/rds.2012.9.6.
Myers, D.J., Wallen, J.M., 2020. Cancer, lung adenocarcinoma. In: StatPearls [Internet].
Nakajima, S., Kabata, H., Kabashima, K., Asano, K., 2020. Anti-TSLP antibodies: targeting a master regulator of type 2 immune responses. Allergol. Int. 69 (2), 197–203. https://doi.org/10.1016/j.alit.2020.01.001.
Negi, P.C., Chauhan, R., Rana, V., Lal, K., 2016. Epidemiological study of non-communicable diseases (NCD) risk factors in tribal district of Kinnaur, HP: a cross-sectional study. Indian Heart J. 68 (5), 655–662.
Nelson, A.E., 2018. Osteoarthritis year in review 2017: clinical. Osteoarthr. Cartil. 26 (3), 319–325. https://doi.org/10.1016/j.joca.2017.11.014.
Nicholas, S.B., Kalantar-Zadeh, K., Norris, K.C., 2015. Socioeconomic disparities in chronic kidney disease. Adv. Chronic Kidney Dis. 22 (1), 6–15. https://doi.org/10.1053/j.ackd.2014.07.002.
Nichols, E., Szoeke, C.E., Vollset, S.E., Abbasi, N., Abd-Allah, F., Abdela, J., et al., 2019. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 18 (1), 88–106.
Niu, X., Chen, J., Gao, J., 2019. Nanocarriers as a powerful vehicle to overcome blood-brain barrier in treating neurodegenerative diseases: focus on recent advances. Asian J. Pharm. Sci. 14 (5), 480–496. https://doi.org/10.1016/j.ajps.2018.09.005.
Nixon, R.A., 2013. The role of autophagy in neurodegenerative disease. Nat. Med. 19 (8), 983–997. https://doi.org/10.1038/nm.3232.
Nowbar, A.N., Gitto, M., Howard, J.P., Francis, D.P., Al-Lamee, R., 2019. Mortality from ischemic heart disease: analysis of data from the world health organization and coronary artery disease risk factors from NCD risk factor collaboration. Circ. Cardiovasc. Qual. Outcomes 12 (6). https://doi.org/10.1161/CIRCOUTCOMES.118.005375.
O'Connor, D.M., Boulis, N.M., 2015. Gene therapy for neurodegenerative diseases. Trends Mol. Med. 21 (8), 504–512. https://doi.org/10.1016/j.molmed.2015.06.001.
Oertel, W., Schulz, J.B., 2016. Current and experimental treatments of Parkinson's disease: A guide for neuroscientists. J. Neurochem. 139. 1471-4159 (Electronic).
Orditura, M., Galizia, G., Sforza, V., Gambardella, V., Fabozzi, A., Laterza, M.M., et al., 2014. Treatment of gastric cancer. World J. Gastroenterol. 20 (7), 1635.
Park, S., Kim, J., Seo, Y., Sung, M., 2012. Effects of diet-induced obesity on colitis-associated colon tumor formation in A/J mice. Int. J. Obes. (Lond) 36 (2), 273–280.
Patel, A., Webster, R., 2016. The potential and value of epidemiology in curbing non-communicable diseases. Glob. Health Epidemiol. Genom. 1.
Pellino, A., Riello, E., Nappo, F., Brignola, S., Murgioni, S., Djaballah, S.A., et al., 2019. Targeted therapies in metastatic gastric cancer: current knowledge and future perspectives. World J. Gastroenterol. 25 (38), 5773–5788. https://doi.org/10.3748/wjg.v25.i38.5773.
Permaul, P., Hoffman, E., Fu, C., Sheehan, W., Baxi, S., Gaffin, J., et al., 2012. Allergens in urban schools and homes of children with asthma. Pediatr. Allergy Immunol. 23 (6), 543–549. https://doi.org/10.1111/j.1399-3038.2012.01327.x.
Pike, C.J., 2017. Sex and the development of Alzheimer's disease. J. Neurosci. Res. 95 (1–2), 671–680. https://doi.org/10.1002/jnr.23827.

Poewe, W., Seppi, K., Tanner, C.M., Halliday, G.M., Brundin, P., Volkmann, J., et al., 2017. Parkinson disease. Nat. Rev. Dis. Primers. 3 (1). https://doi.org/10.1038/nrdp.2017.13, 17013.

Pogacnik, L., Ota, A., Ulrih, N.P., 2020. An overview of crucial dietary substances and their modes of action for prevention of neurodegenerative diseases. Cell 9 (3). https://doi.org/10.3390/cells9030576.

Pohl, F., Kong Thoo Lin, P., 2018. The potential use of plant natural products and plant extracts with antioxidant properties for the prevention/treatment of neurodegenerative diseases: in vitro, in vivo and clinical trials. Molecules 23 (12), 3283. https://doi.org/10.3390/molecules23123283.

Potter, K.J., Scrocchi, L.A., Warnock, G.L., Ao, Z., Younker, M.A., Rosenberg, L., et al., 2009. Amyloid inhibitors enhance survival of cultured human islets. Biochim. Biophys. Acta Gen. Subj. 1790 (6), 566–574. https://doi.org/10.1016/j.bbagen.2009.02.013.

Rahman, I., Athar, M.T., Islam, M., 2020. Type 2 diabetes, obesity, and cancer share some common and critical pathways. Front. Oncol. 10. https://doi.org/10.3389/fonc.2020.600824, 600824.

Recio-Boiles, A., Babiker, H., 2020. Gastric Cancer. StatPearls.

Recio-Boiles, A., Babiker, H.M., 2021. Liver cancer. In: StatPearls [Internet]. Treasure Island. StatPearls Publishing, FL.

Recio-Boiles, A., Waheed, A., Cagir, B., 2019. Cancer, colon. In: StatPearls [Internet].

Reed, T.T., 2011. Lipid peroxidation and neurodegenerative disease. Free Radic. Biol. Med. 51, 1302–1319. https://doi.org/10.1016/j.freeradbiomed.2011.06.027. 1873-4596 (Electronic).

Rivera, J.F., Costes, S., Gurlo, T., Glabe, C.G., Butler, P.C., 2014. Autophagy defends pancreatic β cells from human islet amyloid polypeptide-induced toxicity. J. Clin. Invest. 124 (8), 3489–3500. https://doi.org/10.1172/jci71981.

Rizek, P., Kumar, N., Jog, M.S., 2016. An update on the diagnosis and treatment of Parkinson's disease. Can. Med. Assoc. J. 188 (16), 1157. https://doi.org/10.1503/cmaj.151179.

Rogliani, P., Ora, J., Puxeddu, E., Cazzola, M., 2016. Airflow obstruction: is it asthma or is it COPD? Int. J. Chron. Obstruct. Pulmon. Dis. 11, 3007–3013. https://doi.org/10.2147/COPD.S54927.

Romagnani, P., Remuzzi, G., Glassock, R., Levin, A., Jager, K.J., Tonelli, M., et al., 2017. Chronic kidney disease. Nat. Rev. Dis. Primers. 3 (1), 17088. https://doi.org/10.1038/nrdp.2017.88.

Roth, G.A., Mensah, G.A., Johnson, C.O., Addolorato, G., Ammirati, E., Baddour, L.M., et al., 2020. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J. Am. Coll. Cardiol. 76 (25), 2982–3021. https://doi.org/10.1016/j.jacc.2020.11.010.

Sacco, R.L., Roth, G.A., Reddy, K.S., Arnett, D.K., Bonita, R., Gaziano, T.A., et al., 2016. The heart of 25 by 25: achieving the goal of reducing global and regional premature deaths from cardiovascular diseases and stroke: a modeling study from the American Heart Association and World Heart Federation. Circulation 133 (23), e674–e690.

Salehi, B., Zucca, P., Sharifi-Rad, M., Pezzani, R., Rajabi, S., Setzer, W.N., et al., 2018. Phytotherapeutics in cancer invasion and metastasis. Phytother. Res. 32 (8), 1425–1449. https://doi.org/10.1002/ptr.6087.

Sauter, E.R., 2018. Breast cancer prevention: current approaches and future directions. Eur. J. Breast Health 14 (2), 64.

Sawda, C., Moussa, C., Turner, R.S., 2017. Resveratrol for Alzheimer's disease. Ann. N.Y. Acad. Sci. 1403 (1), 142–149. https://doi.org/10.1111/nyas.13431.

Schreuders, E.H., Ruco, A., Rabeneck, L., Schoen, R.E., Sung, J.J., Young, G.P., Kuipers, E.J., 2015. Colorectal cancer screening: a global overview of existing programmes. Gut 64 (10), 1637–1649.

Screening, P., Board, P.E., 2020. Stomach (gastric) cancer prevention (PDQ®). In: PDQ Cancer Information Summaries [Internet]. National Cancer Institute (US).

Seppi, K., Ray Chaudhuri, K., Coelho, M., Fox, S.H., Katzenschlager, R., Perez Lloret, S., et al., 2019. Update on treatments for nonmotor symptoms of Parkinson's disease—an evidence-based medicine review. Mov. Disord. 34 (2), 180–198. https://doi.org/10.1002/mds.27602.

Shah, N.A., Khan, M.R., Nigussie, D., 2017. Phytochemical investigation and nephroprotective potential of Sida cordata in rat. BMC Complement. Altern. Med. 17 (1), 388. https://doi.org/10.1186/s12906-017-1896-8.

Shahpiri, Z., Bahramsoltani, R., Hosein Farzaei, M., Farzaei, F., Rahimi, R., 2016. Phytochemicals as future drugs for Parkinson's disease: a comprehensive review. Rev. Neurosci. 27 (6), 651–668. https://doi.org/10.1515/revneuro-2016-0004.

Sherr, J., Sosenko, J., Skyler, J.S., Herold, K.C., 2008. Prevention of type 1 diabetes: the time has come. Nat. Clin. Pract. Endocrinol. Metab. 4 (6), 334–343. https://doi.org/10.1038/ncpendmet0832.

Shlomai, G., Neel, B., LeRoith, D., Gallagher, E.J., 2016. Type 2 diabetes mellitus and cancer: the role of pharmacotherapy. J. Clin. Oncol. 34 (35), 4261–4269. https://doi.org/10.1200/jco.2016.67.4044.

Siddiqui, F., Siddiqui, A.H., 2020. Cancer, lung. In: StatPearls [Internet].

Siddiqui, S., Denlinger, L.C., Fowler, S.J., Akuthota, P., Shaw, D.E., Heaney, L.G., et al., 2019. Unmet needs in severe asthma subtyping and precision medicine trials. Bridging clinical and patient perspectives. Am. J. Respir. Crit. Care Med. 199 (7), 823–829. https://doi.org/10.1164/rccm.201809-1817PP.

Singh, S., Jha, H.C., 2017. Status of Epstein-Barr virus coinfection with Helicobacter pylori in gastric cancer. J. Oncol. 2017.

Singh, G.M., Danaei, G., Farzadfar, F., Stevens, G.A., Woodward, M., Wormser, D., et al., 2013. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. PLoS One 8 (7). https://doi.org/10.1371/journal.pone.0065174, e65174.

Škrha, J., 2021. Diabetes, lipids, and CV risk. Curr. Atheroscler. Rep. 23 (3), 8. https://doi.org/10.1007/s11883-021-00905-8.

Solanki, I., Parihar, P., Parihar, M.S., 2016. Neurodegenerative diseases: from available treatments to prospective herbal therapy. Neurochem. Int. 95, 100–108. https://doi.org/10.1016/j.neuint.2015.11.001.

Song, M., Garrett, W.S., Chan, A.T., 2015. Nutrients, foods, and colorectal cancer prevention. Gastroenterology 148 (6), 1244–1260.e1216.

Subramanian, S., Gakunga, R., Kibachio, J., Gathecha, G., Edwards, P., Ogola, E., et al., 2018. Cost and affordability of non-communicable disease screening, diagnosis and treatment in Kenya: patient payments in the private and public sectors. PLoS One 13 (1), e0190113.

Suresh, S., Chhipa, A.S., Gupta, M., Lalotra, S., Sisodia, S.S., Baksi, R., Nivsarkar, M., 2020. Phytochemical analysis and pharmacological evaluation of methanolic leaf extract of Moringa oleifera Lam. in ovalbumin induced allergic asthma. S. Afr. J. Bot. 130, 484–493. https://doi.org/10.1016/j.sajb.2020.01.046.

Suwannaphant, K., Laohasiriwong, W., Puttanapong, N., Saengsuwan, J., Phajan, T., 2017. Association between socioeconomic status and diabetes mellitus: the National Socioeconomics Survey, 2010 and 2012. J. Clin. Diagn. Res. 11 (7), LC18.

Taher, A.-T., AlSayed, A., Alawadi, S., Ibrahim, M., Ashour, W., Jaafar, H., et al., 2016. A multicenter prospective phase II trial of neoadjuvant epirubicin, cyclophosphamide, and 5-fluorouracil (FEC100) followed by cisplatin–docetaxel with or without trastuzumab in locally advanced breast cancer. Cancer Chemother. Pharmacol. 77 (1), 147–153.

Tantucci, C., 2021. Assessment and treatment of airflow obstruction in patients with chronic obstructive pulmonary disorder: a guide for the clinician. Expert Rev. Respir. Med., 1–8. https://doi.org/10.1080/17476348.2021.1851602.

Tantucci, C., Modina, D., 2012. Lung function decline in COPD. Int. J. Chron. Obstruct. Pulmon. Dis. 7, 95–99. https://doi.org/10.2147/copd.s27480.
Tetley, T.D., 2005. Inflammatory cells and chronic obstructive pulmonary disease. Curr. Drug Targets Inflamm. Allergy 4 (6), 607–618. https://doi.org/10.2174/156801005774912824.
The Global Asthma Report, 2018. Global Asthma Network.
Tortora, G.J., Derrickson, B.H., 2018. Principles of Anatomy and Physiology. John Wiley & Sons.
Trowsdale, J., Knight, J.C., 2013. Major histocompatibility complex genomics and human disease. Annu. Rev. Genomics Hum. Genet. 14, 301–323. https://doi.org/10.1146/annurev-genom-091212-153455.
Tsukuma, H., Tanaka, H., Ajiki, W., Oshima, A., 2005. Liver cancer and its prevention. Asian Pac. J. Cancer Prev. 6 (3), 244.
Tysnes, O.-B., Storstein, A., 2017. Epidemiology of Parkinson's disease. J. Neural Transm. 124 (8), 901–905. https://doi.org/10.1007/s00702-017-1686-y.
Unwin, N., Alberti, K., 2006. Chronic non-communicable diseases. Ann. Trop. Med. Parasitol. 100 (5–6), 455–464.
Virani, S.S., Alonso, A., Aparicio, H.J., Benjamin, E.J., Bittencourt, M.S., Callaway, C.W., et al., 2021. Heart disease and stroke statistics—2021 update. Circulation 143 (8), e254–e743. https://doi.org/10.1161/CIR.0000000000000950.
Volk, R.J., Mendoza, T.R., Hoover, D.S., Nishi, S.P., Choi, N.J., Bevers, T.B., 2020. Reliability of self-reported smoking history and its implications for lung cancer screening. Prev. Med. Rep. 17, 101037.
Walters, A.M., Porter, G.A., Brookes, P.S., 2012. Mitochondria as a drug target in ischemic heart disease and cardiomyopathy. Circ. Res. 111 (9), 1222–1236. https://doi.org/10.1161/CIRCRESAHA.112.265660.
Wang, K., Xu, J., Hunter, D.J., Ding, C., 2015. Investigational drugs for the treatment of osteoarthritis. Expert Opin. Investig. Drugs 24 (12), 1539–1556. https://doi.org/10.1517/13543784.2015.1091880.
Wedzicha, J.A., Brill, S.E., Allinson, J.P., Donaldson, G.C., 2013. Mechanisms and impact of the frequent exacerbator phenotype in chronic obstructive pulmonary disease. BMC Med. 11 (1), 181. https://doi.org/10.1186/1741-7015-11-181.
Wenzel, S.E., 2012. Asthma phenotypes: the evolution from clinical to molecular approaches. Nat. Med. 18 (5), 716–725. https://doi.org/10.1038/nm.2678.
Whitney, K.E., Liebowitz, A., Bolia, I.K., Chahla, J., Ravuri, S., Evans, T.A., et al., 2017. Current perspectives on biological approaches for osteoarthritis. Ann. N.Y. Acad. Sci. 1410 (1), 26–43. https://doi.org/10.1111/nyas.13554.
Williams, J., Allen, L., Wickramasinghe, K., Mikkelsen, B., Roberts, N., Townsend, N., 2018. A systematic review of associations between non-communicable diseases and socioeconomic status within low- and lower-middle-income countries. J. Glob. Health 8 (2). https://doi.org/10.7189/jogh.08.020409, 020409.
Wolpin, B.M., Mayer, R.J., 2008. Systemic treatment of colorectal cancer. Gastroenterology 134 (5), 1296–1310.e1291.
World Health Organization, 2010. Global status report on noncommunicable diseases. Retrieved on August 12, 2021 from https://www.who.int/nmh/publications/ncd_report_full_en.pdf.
World Health Organization, 2020, December 09. The top 10 causes of death. Retrieved on August 12, 2021 from https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
World Health Organization, 2021a. Cardiovascular diseases. Retrieved from https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1.
World Health Organization, 2021, April 12. Noncommunicable diseases. Retrieved on August 12, 2021 from https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases.

World Health Organization, 2021, April 13. Diabetes. Retrieved on August 12, 2021 from https://www.who.int/news-room/fact-sheets/detail/diabetes.
World Health Organization, 2021, March 12. Cancer. Retrieved on August 12, 2021 from https://www.who.int/news-room/fact-sheets/detail/cancer.
Wu, Y., Goh, E.L., Wang, D., Ma, S., 2018. Novel treatments for osteoarthritis: an update. Open Access Rheumatol. 10, 135–140. https://doi.org/10.2147/OARRR.S176666.
Xie, M., Liu, J., Tsao, R., Wang, Z., Sun, B., Wang, J., 2019. Whole grain consumption for the prevention and treatment of breast cancer. Nutrients 11 (8). https://doi.org/10.3390/nu11081769.
Xing, G., Woo, A.Y.-H., Pan, L., Lin, B., Cheng, M.-S., 2020. Recent advances in β2-agonists for treatment of chronic respiratory diseases and heart failure. J. Med. Chem. 63 (24), 15218–15242. https://doi.org/10.1021/acs.jmedchem.0c01195.
Yach, D., Hawkes, C., Gould, C.L., Hofman, K.J., 2004. The global burden of chronic diseases: overcoming impediments to prevention and control. JAMA 291 (21), 2616–2622.
Yang, A., Yu, G., Wu, Y., Wang, H., 2021. Role of β2-adrenergic receptors in chronic obstructive pulmonary disease. Life Sci. 265, 118864. https://doi.org/10.1016/j.lfs.2020.118864.
Yoosefian, M., Rahmanifar, E., Etminan, N., 2018. Nanocarrier for levodopa Parkinson therapeutic drug; comprehensive benserazide analysis. Artif. Cells Nanomed. Biotechnol. 46 (Suppl. 1), 434–446. https://doi.org/10.1080/21691401.2018.1430583.
Zappa, C., Mousa, S.A., 2016. Non-small cell lung cancer: current treatment and future advances. Transl. Lung Cancer Res. 5 (3), 288.
Ziegler, A.G., Nepom, G.T., 2010. Prediction and pathogenesis in type 1 diabetes. Immunity 32 (4), 468–478. https://doi.org/10.1016/j.immuni.2010.03.018.
Zvěřová, M., 2019. Clinical aspects of Alzheimer's disease. Clin. Biochem. 72, 3–6. https://doi.org/10.1016/j.clinbiochem.2019.04.015.