Exploration of Medicine

Open Exploration

Open Access Review

The viral oncogenesis of COVID-19 and its impact on cancer progression, long-term risks, treatment complexities, and research strategies

Moawiah M Naffaa[1,2†*], Ola A Al-Ewaidat[3†]

[1]Department of Psychology and Neuroscience, Duke University, Durham, NC 27708, USA
[2]Department of Cell Biology, Duke University School of Medicine, Durham, NC 27710, USA
[3]Department of Internal Medicine, Ascension Saint Francis Hospital, Evanston, IL 60202, USA

[†]These authors contributed equally to this work.
***Correspondence:** Moawiah M Naffaa, Department of Psychology and Neuroscience, Duke University, Durham, NC 27708, USA. Moawiah.naffaa@duke.edu
Academic Editor: Haim Werner, Tel Aviv University, Israel
Received: January 9, 2025 **Accepted:** April 17, 2025 **Published:** April 28, 2025

Cite this article: Naffaa MM, Al-Ewaidat OA. The viral oncogenesis of COVID-19 and its impact on cancer progression, long-term risks, treatment complexities, and research strategies. Explor Med. 2025;6:1001314. https://doi.org/10.37349/emed.2025.1001314

Abstract

The interaction between cancer and coronavirus disease 2019 (COVID-19) poses significant challenges, particularly for immunocompromised individuals who are at heightened risk for acute infections and long-term complications. The pandemic has exacerbated existing vulnerabilities in cancer care by disrupting treatment protocols and delaying diagnoses, leading to worsened health outcomes. This article emphasizes the importance of investigating the potential impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on cancer progression and highlights the need for effective strategies to protect this high-risk population. Long-term health consequences, including the emergence of long COVID, further emphasize the need for ongoing surveillance and comprehensive healthcare planning for cancer patients during and after pandemics. A multifaceted approach is essential, incorporating vaccination, timely therapeutic interventions, and sustained support for patients with lingering symptoms. This article also discusses and urges continued research into the oncogenic risks associated with SARS-CoV-2, which is crucial for enhancing our understanding of the broader health implications of COVID-19 and for informing public health strategies aimed at safeguarding cancer patients in future pandemics. Moreover, effective data collection and the development of refined clinical guidelines are vital for improving patient outcomes and preparing healthcare systems to support cancer patients during crises. Additionally, this article discusses the importance of investigating the mechanisms by which SARS-CoV-2 may increase cancer susceptibility, including chronic inflammation, cellular senescence, and immune dysregulation. Understanding these mechanisms is crucial for elucidating the virus's long-term oncogenic potential, particularly among cancer survivors and individuals with chronic infections. Ensuring continuity and resilience in cancer care during global crises requires strategies to mitigate healthcare disruptions, enhance access to screenings and treatments, and address the specific challenges faced by cancer patients experiencing long COVID.

Keywords

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), coronavirus disease 2019 (COVID-19), viral oncogenesis, cancer patients, long COVID-19, long-term cancer risk, immune dysregulation, cancer development

Introduction: the intersection of COVID-19 and cancer—implications for patient vulnerability, disease progression, and oncogenic potential

The COVID-19 pandemic has posed unprecedented challenges to global healthcare systems, disproportionately affecting vulnerable populations, including cancer patients [1, 2]. Studies have consistently shown that individuals with cancer are at a heightened risk of contracting SARS-CoV-2 and experiencing more severe disease outcomes, including increased mortality and complications [3, 4]. This vulnerability is attributed to a combination of factors, including advanced age, preexisting comorbidities, and the immunosuppressive effects of cancer itself and its treatments, such as chemotherapy and radiotherapy [5, 6]. However, data on the precise influence of cancer type and treatment regimens on COVID-19 outcomes remain inconsistent, highlighting the need for further investigation.

Patients suffering from various diseases, particularly those related to cerebrovascular conditions and stroke, have also shown significant impacts from COVID-19 in multiple ways [7, 8]. Studies have already explored these connections, and further research holds promise for clarifying and addressing these links. This could play a crucial role in protecting vulnerable patient groups from severe outcomes associated with COVID-19 infections.

Beyond the immediate clinical risks, the pandemic has significantly disrupted cancer care. Delays in diagnoses, screenings, and treatments have led to an increase in advanced-stage cancer cases, potentially worsening long-term survival rates [9, 10]. Healthcare providers have faced difficult decisions in balancing the urgency of cancer treatment with the risks of SARS-CoV-2 exposure in immunocompromised patients [11, 12]. While vaccines and therapeutic advancements have facilitated a return to standard care, managing cancer in the context of COVID-19 remains a persistent challenge [10, 13].

The relationship between viral infections and cancer is well established, with several viruses, including human papillomavirus (HPV), hepatitis B and C (HBV, HCV), and Epstein-Barr virus (EBV), recognized as oncogenic agents [14–16]. These viruses contribute to tumorigenesis by interfering with tumor suppressor genes, promoting chronic inflammation, or inducing immune evasion. Emerging evidence suggests that coronaviruses, including SARS-CoV-1 and Middle East respiratory syndrome coronavirus (MERS-CoV), may interact with cancer-related pathways. These interactions could potentially influence oncogenesis through mechanisms such as oxidative stress, immune dysregulation, and disruption of cell cycle regulation [14, 15]. SARS-CoV-1, for instance, has been shown to repress the tumor suppressor protein retinoblastoma (pRB) and interfere with cell-cell contact inhibition, raising concerns about whether SARS-CoV-2 might exert similar oncogenic effects [17, 18].

Long-term complications of SARS-CoV-2 infection, commonly referred to as post-acute sequelae of SARS-CoV-2 infection (PASC) or long COVID, have further implications for cancer patients [18]. Chronic inflammation, persistent immune dysfunction, and cellular stress—hallmarks of long COVID—may create a microenvironment conducive to tumorigenesis [19–21]. While direct evidence linking SARS-CoV-2 to cancer remains preliminary, these potential mechanisms warrant further investigation, particularly given the long-term health implications of the virus.

Understanding the interplay between COVID-19 and cancer is essential for guiding future research and healthcare policies. While observational studies have begun to explore potential connections, significant gaps remain due to limitations in data generalizability and comprehensiveness. Determining whether SARS-CoV-2 directly or indirectly influences cancer development and progression requires extensive, in-depth research to clarify the underlying mechanisms.

This study aims to investigate the impact of SARS-CoV-2 infection, including acute COVID-19 and long COVID, on cancer progression, focusing on how immune dysregulation and genetic alterations contribute to oncogenesis. Additionally, it explores the distinct clinical outcomes observed in cancer patients, which result from the complex interplay between their malignancy, ongoing treatments, and viral pathophysiology. To address these issues, this article analyzes the challenges faced by cancer patients with acute and long-term COVID-19, particularly in symptom management and treatment complexities. Additionally, it examines the potential role of SARS-CoV-2 in cancer development and its long-term oncogenic risk. Furthermore, it investigates the genetic and immunological mechanisms underlying viral oncogenesis, with a specific focus on how SARS-CoV-2 may promote cancer progression. The study also assesses the variability in COVID-19 outcomes among cancer patients based on cancer type and treatment regimens. Furthermore, it proposes key strategies for advancing research on cancer care during global health crises, including addressing healthcare disruptions, treatment delays, and the prolonged effects of COVID-19. Ultimately, this work aims to provide a comprehensive understanding of the relationship between COVID-19 and cancer progression, highlighting the need for targeted clinical approaches to mitigate risks in cancer patients. By shaping future research priorities and healthcare policies, this study aims to enhance the resilience of cancer care during pandemics. Additionally, it evaluates the oncogenic potential of SARS-CoV-2 and recommends necessary adaptations in oncology practice to address emerging viral threats.

Persistent symptoms and treatment complexities in cancer patients with acute COVID-19 and long COVID

Given the continued global impact of cancer as a major public health challenge, understanding the interplay between cancer and COVID-19 is essential. Research has already investigated how COVID-19 affects cancer outcomes, associated risk factors, and healthcare disruptions (Table 1); however, further studies are required to deepen this understanding. For instance, a large cohort study analyzed electronic health records (EHRs) from over 500,000 adults, comparing outcomes such as mortality, ICU admissions, mechanical ventilation, and hospitalizations between patients with and without cancer [22]. In fully adjusted models, cancer patients receiving recent treatments exhibited an increased 30-day risk of death, ICU stays, and hospitalization. Conversely, cancer patients without recent treatment had comparable risks of mortality and ICU admission to non-cancer patients, though their risk of mechanical ventilation and hospitalization remained lower [22]. These findings underscore the importance of risk stratification based on recent treatments, highlighting the complexities of managing cancer care during the pandemic.

Table 1. COVID-19 and cancer: outcomes, risk factors, and healthcare disruptions

Topic	Details/Findings	References
Cancer and COVID-19 outcomes	Recent cancer treatment increased mortality, ICU admission, and hospitalization risks, while untreated patients had mortality rates similar to non-cancer individuals.	[22, 23]
Risk factors for severe COVID-19	Older age, comorbidities, male sex, severe obesity, and racial/ethnic background heightened mortality risk.	[4, 24]
Impact on cancer care	The pandemic disrupted screenings and treatments; delayed colorectal cancer surgery increased mortality by 13%.	[25]
Cancer research disruptions	One-third of clinical trials were delayed or halted, and two-thirds of research labs closed, setting back discoveries by up to 18 months. HPV vaccination declines may raise future cancer risks.	[26]
Mortality risk in hospitalized patients	Cancer patients accounted for 10% of hospitalized COVID-19 cases and had higher in-hospital mortality. Younger cancer patients faced disproportionately high mortality.	[27, 28]
Vaccine efficacy	Cancer patients, especially those with hematologic malignancies, showed reduced vaccine efficacy. The delta variant widened the mortality gap.	[29, 30]
ICU admission trends	Cancer patients were generally less likely to be admitted to the ICU, except for younger patients, whose ICU admission rates matched non-cancer peers despite higher mortality.	[30–32]
Long COVID in cancer patients	Nearly 50% of cancer survivors developed long COVID, commonly experiencing fatigue, sleep disturbances, and muscle pain. Women were more affected, and initial infection severity did not predict long COVID risk.	[33–35]

COVID-19: coronavirus disease 2019; HPV: human papillomavirus

One potential research direction involves conducting longitudinal studies on individuals who have recovered from COVID-19 to assess cancer incidence over time. Given the inflammatory nature of SARS-CoV-2 and its effects on critical tumor suppressor genes [36], monitoring cancer rates in these survivors could help clarify any causal relationship between the virus and cancer development.

Cancer patients tend to be older and have more comorbidities than the general population, both of which are associated with adverse COVID-19 outcomes [22, 37]. Additional risk factors identified include male sex, severe obesity, and certain racial and ethnic backgrounds. Broader research has similarly emphasized the role of biological and socioeconomic factors in determining COVID-19 severity in both cancer and non-cancer patients [38]. For example, non-Hispanic Black patients did not exhibit an increased mortality risk after adjusting for comorbidities, highlighting the need for further investigation into how race and ethnicity influence health outcomes [39].

After accounting for factors such as age and comorbidities, mortality rates between cancer and non-cancer patients may be comparable. Studies, such as the Lean European Open Survey on SARS-CoV-2 Infected Patients (LEOSS) registry, reported similar mortality rates between these groups once confounding factors were controlled, emphasizing the complex interplay of factors influencing COVID-19 outcomes [40].

The COVID-19 pandemic has had profound and far-reaching indirect effects on healthcare, particularly in the prevention and treatment of cancer [41]. Research highlights how the pandemic impacted cancer incidence and mortality, primarily through significant disruptions in healthcare services. These disruptions led to delays in cancer screening, diagnosis, and treatment, potentially reversing recent declines in cancer mortality rates [42]. For example, a study found that a one-year disruption, including a 26-week delay in treatment, could result in an additional 1,719 colorectal cancer (CRC) deaths in Australia between 2020 and 2044 [43]. Early detection through screenings is vital, particularly for cancers like colorectal, breast, and melanoma, but many countries postponed screenings during the pandemic [44]. Treatment delays also worsened outcomes; for example, a four-week delay in colon cancer surgery increases mortality risk by 6%, and delayed chemotherapy raises CRC mortality risk by 13% [45]. In Canada, average treatment initiation times for cancer patients increased from 4.5 weeks pre-pandemic to 44 days, significantly elevating death risks for those affected [46].

The pandemic also disrupted cancer research, with a third of clinical trials delayed or stopped, and two-thirds of labs closed, potentially delaying breakthroughs by 18 months [47]. Globally, public health campaigns like HPV vaccination were also interrupted, reducing coverage and increasing future cancer risks. For example, HPV vaccination rates in the UK dropped from 88% to 59%, and projections in the United States suggest up to 6,200 additional oropharyngeal cancer cases by 2100 due to the disruption [48].

The long-term impact of the pandemic on cancer care, emphasizing the need for future public health planning to address these indirect consequences. Understanding how large-scale crises reshape healthcare is essential for preparing for future emergencies and ensuring recovery in cancer care.

Early studies during the COVID-19 pandemic highlighted the heightened vulnerability of cancer patients. In the UK, it was found that 10% of hospitalized COVID-19 patients had a history of cancer, and this group exhibited a significantly higher in-hospital mortality rate compared to non-cancer patients [49]. The hazard ratio (HR) of 1.13 further underscored the increased risk faced by this demographic [50, 51]. This elevated mortality risk emphasizes the severity of COVID-19 outcomes in cancer patients and highlights the unique challenges they face, including delayed cancer treatments due to hospital resource shortages, disruption of ongoing cancer therapies, and lack of timely access to necessary diagnostic services [52]. For instance, during the pandemic, many oncology departments had to postpone elective surgeries, radiation treatments, and even chemotherapy regimens, leading to exacerbated disease progression [53, 54]. In some cases, these delays were further compounded by overwhelmed healthcare systems that struggled to manage both COVID-19 patients and cancer care. Additionally, cancer patients often face difficulty accessing routine imaging and laboratory diagnostics, which are essential for monitoring disease progression and making timely adjustments to treatment plans [55].

Moreover, the shortage of hospital beds, especially during peak COVID-19 surges, resulted in cancer patients being displaced from specialized cancer care units to general wards [1, 56], where the quality of care could be suboptimal for their specific needs. This reallocation of resources hindered the ability to deliver timely and appropriate interventions for cancer patients, worsening prognosis in many cases.

Additionally, many cancer patients experienced the compounding effect of being unable to receive routine care or attend cancer screenings, which resulted in delayed diagnoses and worsened outcomes [57]. The pandemic also led to the cancellation or postponement of cancer screening programs, such as mammograms and colonoscopies, which are critical for early detection of various cancers. This disruption in screening services has likely led to a surge in cancer diagnoses at more advanced stages, which are more difficult to treat and have worse survival rates. Moreover, the healthcare system's overwhelming focus on COVID-19 cases led to an inadequate allocation of resources for cancer treatment centers, which worsened survival prospects for cancer patients. In some countries, cancer treatment units were repurposed as intensive care units for COVID-19 patients, deprioritizing ongoing cancer care [41, 53, 58]. This has significantly impacted patient outcomes, as the delay in critical treatments, such as immunotherapy or hormone therapy, can substantially alter the course of the disease.

Further investigations into age and cancer treatment outcomes revealed that although older cancer patients experienced worse absolute outcomes, younger cancer patients exhibited a disproportionately higher relative mortality risk when compared to non-cancer patients of the same age [59]. This observation challenges the prevailing belief that older age alone is the most significant factor in severe COVID-19 outcomes. Several factors, including cancer type, treatment intensity, and social interactions, may contribute to the elevated risk observed in younger cancer patients [60].

In regard to vaccination, despite the overall reduction in mortality due to vaccination, the efficacy of the vaccines was found to be lower in cancer patients, especially those with hematological malignancies [13, 29]. The delta variant surge in 2021 further widened the mortality gap between cancer patients and the general population, underscoring the need for targeted protective measures. Data spanning the pandemic, from the initial wave to the early Omicron variants (BA.1 and BA.2), illustrated how shifting variants, societal changes like the relaxation of lockdowns, and varying vaccine effectiveness influenced mortality risks over time [61].

In terms of ICU admissions, cancer patients were generally less likely to be escalated to the ICU compared to non-cancer patients [32]. However, this pattern was not observed in younger cancer patients, who, despite their increased mortality risk, were admitted to the ICU at similar rates to non-cancer patients [30]. This disparity suggests that factors beyond ICU admission rates may contribute to poor outcomes among cancer patients. This highlights the need for a more detailed exploration of ICU decision-making and the underlying causes of these outcomes [62].

The findings highlight the need for continued research into ICU escalation decisions and the specific drivers of poor outcomes for cancer patients admitted to the ICU with COVID-19. A more nuanced understanding of these elements could inform clinical guidelines, ultimately improving care and outcomes for this particularly vulnerable population [63].

Looking ahead, it is clear that cancer patients remain at high risk from COVID-19, necessitating ongoing mitigation efforts. These should include prioritizing vaccination for this group, regular testing of healthcare staff in high-risk environments, and ensuring timely access to antiviral treatments and therapeutic antibodies [64]. In the context of future pandemics, the study emphasizes the importance of systematic data collection for cancer patients, advocating for the use of national protocols to provide a comprehensive understanding of their specific risks. This approach would offer more robust insights than isolated cancer registries and would enhance preparedness and response strategies for high-risk groups.

Future clinical research on the impact of COVID-19 on cancer patients is essential for understanding and addressing their increased vulnerability to severe outcomes. Studies consistently show that cancer patients are at higher risk of adverse effects from COVID-19, influenced by factors such as pre-existing comorbidities, cancer stage, ongoing treatments, and immunosuppression [4, 65].

While the immediate effects of COVID-19 on multiple organ systems have been well documented, there is growing concern about the persistence of symptoms long after recovery, especially among cancer patients. Research draws parallels between long COVID and post-viral syndromes observed after past outbreaks [66, 67]. Long COVID, or post-acute sequelae of SARS-CoV-2 (PASC), is characterized by symptoms persisting for at least four weeks after diagnosis. Estimates of its prevalence in the general population vary widely, from 10% to around 90%, but data specific to cancer patients are limited, and the implications for their care and prognosis remain unclear [68, 69].

The severity of the initial COVID-19 infection appears to be a key factor in the development of long COVID, with patients who required hospitalization more likely to experience lingering symptoms. However, even those with mild or moderate infections have reported prolonged health issues, underscoring the complexity of the condition [70]. A study of few hundreds' cancer patients found that 60% developed long COVID, with women more likely to report symptoms such as fatigue, sleep disturbances, and muscle pain. Surprisingly, cancer type, age, or initial infection severity did not predict long COVID, although hypertension was inversely associated with its development [33]. Hypertension, a known risk factor for severe acute COVID-19, appears to have a different role in long COVID, suggesting distinct mechanisms between the acute and post-acute phases of the disease. Furthermore, although men typically experience more severe COVID-19, women in this study were more likely to report long-term symptoms, pointing to possible influences from immune responses and hormonal factors [34, 71].

Fatigue was the most commonly reported symptom in cancer patients with long COVID, affecting 82%, consistent with reports from the general population. Other prevalent symptoms included sleep disturbances, muscle pain, and gastrointestinal issues. However, ongoing cancer treatments such as chemotherapy and radiotherapy may complicate symptom attribution, making it difficult to determine whether these are related to COVID-19 or cancer therapy [72, 73].

Long COVID poses significant concerns for cancer patients, particularly women, with fatigue and sleep disturbances being the most frequent symptoms [33, 74]. Although severe acute COVID-19 was associated with higher mortality, it did not reliably predict the development of long COVID [75]. Further research is critical to developing effective long-term management strategies tailored to the specific needs of cancer patients.

The molecular impact of SARS-CoV-2 on cancer development

SARS-CoV-2, the virus responsible for COVID-19, is a positive-sense, single-stranded RNA (ss-RNA) virus with a genome size of 26–32 kilobases [76]. Unlike retroviruses, which encode reverse transcriptase, SARS-CoV-2 does not have the capacity to convert RNA into DNA. However, it possesses critical molecular components, including the spike (S) protein, which enables viral entry into human cells. The receptor-binding domain (RBD) of the spike protein, located in the S1 subunit, interacts specifically with angiotensin-converting enzyme 2 (ACE2) receptors on human cell surfaces, facilitating viral invasion (Table 2) [77, 78]. Mutations in the spike protein, particularly within the RBD, can impair antibody recognition, increasing the risk of reinfection and diminishing vaccine efficacy.

Table 2. The molecular mechanisms of SARS-CoV-2 and its potential role in cancer development

Molecular mechanism	Description	Potential impact on cancer	Reference
Spike (S) protein and ACE2 interaction	The spike protein binds ACE2, facilitating viral entry.	ACE2 downregulation disrupts RAAS, promoting inflammation, fibrosis, and cancer progression.	[79, 80]
CircRNAs and miRNA interaction	SARS-CoV-2 circRNAs interact with host miRNAs.	Alters metabolic and tumorigenic pathways, potentially affecting cancer-related processes.	[81–84]
Dysregulation of renin-angiotensin-aldosterone system (RAAS)	ACE2 downregulation disrupts Ang-2/AT1R signaling.	Enhances inflammation, cancer stem cell formation, and oncogenic pathways (e.g., MAPK/ERK, TGF-β, IL-6, IL-8), driving tumor growth and metastasis, particularly in NSCLC.	[85–88]
Tumor suppressor degradation (pRB, p53)	Viral proteins (e.g., nsp15, nsp3) degrade pRB and p53.	Loss of tumor suppressors leads to uncontrolled cell proliferation and increased cancer risk.	[89–92]

Table 2. The molecular mechanisms of SARS-CoV-2 and its potential role in cancer development (*continued*)

Molecular mechanism	Description	Potential impact on cancer	Reference
Epigenetic modifications	SARS-CoV-2 proteins interact with epigenetic regulators (e.g., nsp7, nsp8, nsp14, SIRT5, and NSD2).	Alters gene expression; NSD2 activates RAS signaling, while SIRT5/HDAC2 modulate p53 and tumor progression.	[93–96]
Cytokine storm and inflammatory pathways	Severe COVID-19 triggers elevated IL-6 and other cytokines.	STAT3/NF-κB activation promotes proto-oncogene expression (e.g., c-myc), fueling tumor growth and metastasis.	[88, 97–100]
Viral-host protein interactions	SARS-CoV-2 proteins modulate host pathways.	Potential activation of oncogenic Wnt and NF-κB signaling, suggesting therapeutic targets.	[36, 98, 101, 102]

ACE2: angiotensin-converting enzyme 2; Ang-2: angiopoietin-2; circRNAs: circular RNAs; COVID-19: coronavirus disease 2019; miRNA: microRNA; NSCLC: non-small cell lung cancer; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; pRB: protein retinoblastoma

Circular RNAs (circRNAs) and the molecular intersection of viral and cancer pathways

Beyond its immediate impact on the respiratory system, SARS-CoV-2 may influence broader biological processes that could contribute to cancer development [103]. Recent studies have identified virus-encoded circular RNAs (circRNAs) in various coronaviruses, including SARS-CoV-2, which interact with human microRNAs (miRNAs) (Table 2). These interactions regulate gene networks involved in critical processes such as cancer, metabolism, and autophagy [104]. Specifically, circRNAs derived from MERS-CoV modulate tumorigenic pathways, while SARS-CoV-2-associated circRNAs have been implicated in metabolic and oxidative stress pathways. While oncogenic mechanisms have been observed in SARS-CoV-1, long-term studies have yet to definitively link the virus to cancer development [82, 84]. Although SARS-CoV-2 exhibits characteristics common to oncogenic viruses, definitive evidence connecting it to tumorigenesis remains lacking, necessitating further investigation.

The molecular interactions between SARS-CoV-2 proteins and tumor suppressors or oncogenes represent a crucial area of investigation. Research into how proteins like nsp15 and nsp3 degrade critical tumor suppressors like pRB and p53 could offer valuable insights into the mechanisms of viral oncogenesis [105]. Furthermore, exploring the role of virus-encoded circRNAs in regulating cancer-related gene networks could uncover novel therapeutic targets. The association between SARS-CoV-2 and metabolic and oxidative stress pathways, particularly through circRNAs, also warrants further exploration.

Dysregulation of the renin-angiotensin-aldosterone system (RAAS)

A major area of concern in the context of SARS-CoV-2 infection is its effect on the renin-angiotensin-aldosterone system (RAAS). SARS-CoV-2 downregulates ACE2, a key regulatory protein in RAAS, leading to an imbalance that enhances angiopoietin-2 (Ang-2)/AT1R signaling [106]. This dysregulation contributes to inflammation, fibrosis, and oxidative stress, all of which are recognized as key factors in cancer progression. Ang-2, for instance, has been implicated in the formation of cancer stem cells, particularly in non-small cell lung cancer (NSCLC) (Table 2) [107, 108]. Moreover, Ang-2 activates the MAPK/ERK pathway, resulting in TGF-β production, which further promotes cancer cell growth and migration [109]. Additionally, dysregulated RAAS stimulates the release of inflammatory cytokines like IL-6 and IL-8, as well as vascular endothelial growth factor (VEGF), crucial for tumor angiogenesis [110, 111].

A promising research direction involves understanding how SARS-CoV-2-induced dysregulation of the RAAS influences cancer development, for instance, by enhancing store-operated calcium entry [112, 113]. This line of investigation could provide further insights into the mechanistic links between RAAS disruption and cancer progression. Given the established connection between RAAS and cancer progression, exploring how RAAS imbalances affect cancer stem cell formation and tumor growth could lead to innovative therapeutic strategies. Additionally, assessing inflammatory cytokine levels, such as IL-6 and IL-8, in cancer patients with a history of SARS-CoV-2 infection may improve our understanding of cancer outcomes in COVID-19 survivors.

Impact on tumor suppressors and oncogenes

SARS-CoV-2 also appears to interfere with critical tumor suppressors, such as pRB and p53, through viral proteins like nsp15 and nsp3. These proteins promote the degradation of these tumor suppressors, potentially increasing the risk of cancer (Table 2) [105, 114]. Moreover, viral infections such as SARS-CoV-2 can disrupt the cell cycle and activate pro-apoptotic mechanisms, including the production of caspase-8 (Cas8), further contributing to oncogenesis [88].

Epigenetic and metabolic disruptions

The interaction between SARS-CoV-2 and epigenetic or metabolic regulators is emerging as a critical area of research. SARS-CoV-2 proteins such as nsp7 and nsp8 have been shown to interact with epigenetic modifiers, while nsp14 engages with SIRT5, a protein associated with lung cancer progression [94, 115]. Another epigenetic regulator, NSD2, upregulates the RAS signaling pathway, directly linked to cancer progression (Table 2). Simultaneously, HDAC2, an enzyme that activates the tumor suppressor p53, has been implicated in various cancers, suggesting that the virus may modulate epigenetic pathways influencing tumorigenesis [116, 117].

Epigenetic alterations induced by viral infections represent a critical avenue for further exploration. Specifically, investigating DNA methylation changes linked to cancer risk can yield important insights. By utilizing bisulfite sequencing to profile DNA methylation changes in leukocytes from COVID-19 patients and comparing these profiles to those of healthy controls [118], researchers can identify specific epigenetic modifications that may predispose individuals to cancer.

The potential influence of SARS-CoV-2 proteins on epigenetic regulators like SIRT5 and HDAC2 also presents an exciting frontier in cancer research. Since epigenetic modifications significantly impact gene expression and tumor behavior, investigating how SARS-CoV-2 proteins affect these pathways could provide critical insights into cancer therapy and prevention.

Furthermore, functional studies are needed to determine the effect of these methylation changes on gene expression related to cancer. This research will advance our understanding of how viral infections may influence gene regulation and contribute to oncogenesis.

Cytokine storms and cancer progression

A hallmark feature of severe COVID-19 is the cytokine storm, characterized by elevated levels of pro-inflammatory cytokines such as IL-6. These elevated levels correlate with poor disease outcomes in COVID-19 and may also promote cancer progression (Table 2) [97, 119]. IL-6 activates the STAT3 and NF-κB pathways, which in turn promote the expression of proto-oncogenes like c-myc, driving growth and metastasis in cancers such as pancreatic and breast cancer [87, 98]. This connection between inflammatory responses and cancer progression underscores the need for ongoing research into the long-term oncogenic potential of SARS-CoV-2, especially in individuals who have experienced chronic infection or severe inflammatory responses.

Tumorigenic pathways of SARS-CoV-2: comparative analysis and omics-based investigations

Comparative studies of SARS-CoV-2 alongside established oncogenic viruses such as Epstein-Barr virus (EBV) and human T-cell lymphotropic virus (HTLV) offer valuable opportunities to explore shared and distinct mechanisms of oncogenesis (Table 2) [89]. Identifying common pathways and unique interactions may uncover potential therapeutic targets and inform cancer prevention strategies specific to SARS-CoV-2.

Additionally, the application of integrative omics approaches is crucial for unraveling the virus's impact on cellular processes. By analyzing genetic, transcriptomic, proteomic, and metabolomic profiles in SARS-CoV-2-infected cells, researchers can identify novel biomarkers and pathways linked to the virus's oncogenic potential. Such discoveries are essential for building a comprehensive understanding of the long-term health implications of COVID-19, including its possible contributions to cancer development [120].

A key area of focus is investigating the role of specific viral proteins in modulating cancer-related cellular pathways. Using advanced molecular biology techniques such as CRISPR/Cas9 and RNA interference (RNAi) to knock down viral proteins in cell lines allows for the assessment of their influence on crucial oncogenic pathways, including Wnt and NF-κB signaling. Concurrently, proteomic analyses can identify host proteins that interact with viral components, shedding light on the mechanisms through which these interactions drive tumorigenic processes. These insights may reveal novel targets for therapeutic interventions aimed at cancer prevention in the context of SARS-CoV-2.

Mendelian randomization and the oncogenic potential of SARS-CoV-2: unraveling causal links between viral infections and cancer

The mutagenic effects of SARS-CoV-2 provide a unique insight into the complex relationships between viral infections, immune responses, and oncogenesis [121]. A key tool for studying these connections is Mendelian randomization (MR), an epidemiological method that uses genetic variants as instrumental variables to infer causal relationships between exposures, such as viral infections, and outcomes like cancer risk [122, 123]. MR helps minimize confounding factors and reverse causality, offering a more robust method to establish causality in epidemiological studies. This approach has been previously applied to identify associations between COVID-19 and various chronic conditions, including type 2 diabetes, and cancer risk factors like alterations in gut microbiota and autoimmune diseases such as rheumatoid arthritis [124, 125]. Recent applications of MR to explore potential links between COVID-19 and cancer have provided important insights into how viral infections might contribute to oncogenesis [123].

Recent MR studies have begun to identify genetic predispositions that link COVID-19 with specific cancers (Table 3). For instance, lung adenocarcinoma has emerged as one of the cancers potentially associated with SARS-CoV-2 infection. Genetic data from critically ill and hospitalized COVID-19 patients suggest that cancer risk may increase with the severity of the disease [126, 127]. Critically ill patients demonstrate an elevated risk for cancers such as HER2-positive breast cancer, esophageal cancer, CRC, stomach cancer, and colon cancer [128]. Notably, even patients with less severe disease—those hospitalized but not requiring intensive care—show increased risks for HER2-positive breast cancer, esophageal cancer, and stomach cancer [129].

An intriguing discovery is that individuals with milder SARS-CoV-2 infections, who do not require hospitalization, exhibit a higher risk of stomach cancer, while their risk of head and neck cancer is relatively lower [152, 153]. These variations suggest that the immune response to SARS-CoV-2, even in milder cases, may paradoxically foster an inflammatory environment that supports oncogenesis.

The relationship between COVID-19 severity and cancer risk is multifaceted and, at times, counterintuitive. Milder COVID-19 cases have been linked to an increased risk of gastric cancer, possibly due to immune responses that manage viral replication but cause chronic inflammation in the gastric mucosa [154, 155]. Chronic inflammation is known to promote mutagenic environments, increasing the likelihood of DNA damage and cellular changes that predispose tissues to malignant transformation [99, 156]. Furthermore, the immune dysregulation triggered by SARS-CoV-2 infection may interfere with normal tumor-suppressive mechanisms, contributing to cancer development (Table 3).

Lung cancer

Lung cancer risk among COVID-19 patients is especially concerning due to the direct impact of the virus on the lungs. SARS-CoV-2 induces pulmonary interstitial fibrosis, a well-known precursor to lung malignancies [157]. The virus also activates oncogenic signaling pathways, including the PI3K/AKT pathway, which promotes abnormal proliferation of alveolar epithelial cells. This leads to pathological changes such as hyperplasia and fibrosis, which are risk factors for lung cancer [158, 159].

Additionally, SARS-CoV-2 suppresses immune surveillance by depleting natural killer (NK) cells and cytotoxic T lymphocytes (CTLs), both critical for eliminating cancer cells [160]. This immune impairment, coupled with cytokine storms and chronic inflammation in severe COVID-19, creates a tumor-promoting

Table 3. Genetic associations between COVID-19 and cancer with underlying mechanisms

Cancer type	Genetic link to COVID-19	Mechanisms/Pathophysiology	Reference
Lung cancer	Increased risk, particularly in severe cases.	- SARS-CoV-2 induces pulmonary fibrosis. - Activates oncogenic pathways (e.g., PI3K/AKT), promoting cell proliferation. - Depletes immune cells (NK cells, CTLs), impairing immune defense.	[130–132]
Breast cancer	Linked to HER2-positive cases in severe infections.	- Viral hyperglycosylation disrupts protein interactions. - E-Cadherin downregulation facilitates EMT and invasiveness. - NF-κB activation drives inflammation and tumor progression.	[112, 133, 134]
Pancreatic cancer	Potential modulation of tumorigenesis-related genes.	- Upregulation of PTEN, CREB1, CASP3, and SMAD3. - Chronic inflammation fosters oncogenesis and delays diagnosis.	[135–137]
CRC	COVID-19-induced gut microbiota dysregulation.	- Dysbiosis weakens mucosal immunity. - Chronic inflammation exacerbates mucosal damage, increasing CRC risk.	[138–141]
Oral cancer	Altered angiogenesis and extracellular matrix regulation.	- SARS-CoV-2 modulates angiopoietin-2 and EMMPRIN, promoting tumor growth and metastasis.	[88, 142, 143]
Gastric cancer	Higher incidence in critically ill patients.	- Prolonged viral replication in the GI tract via ACE2 receptors.	[144–147]
Head and neck cancer	Lower risk, potentially due to reduced TMPRSS2 expression.	- Limited viral entry minimizes cellular damage and oncogenesis.	[148–151]

ACE2: angiotensin-converting enzyme 2; COVID-19: coronavirus disease 2019; CRC: colorectal cancer; CTLs: cytotoxic T lymphocytes; EMMPRIN: extracellular matrix metalloproteinase inducer; EMT: epithelial-mesenchymal transition; NK: natural killer; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

environment. The generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) further damages DNA, fueling mutations that drive lung cancer [161, 162]. Elevated cytokines, particularly IL-6, are implicated in metastasis and epithelial-mesenchymal transition (EMT), both hallmarks of aggressive lung cancer.

Breast cancer

SARS-CoV-2 has been linked to an increased risk of HER2-positive breast cancer, potentially through viral hyperglycosylation mechanisms that disrupt cellular protein interactions, downregulating E-cadherin, a molecule crucial for epithelial cell integrity [163, 164]. Loss of E-cadherin facilitates EMT, promoting invasiveness and metastasis. Additionally, the NF-κB pathway, central to inflammation and cancer progression, is activated by SARS-CoV-2, which may enhance breast cancer risk. Interactions between the virus and the ACE2 receptor, a viral entry point, might also unintentionally suppress immune responses [134], further supporting tumor progression in patients with underlying breast cancer.

Severely ill or hospitalized COVID-19 patients are also at increased risk of developing HER2-positive breast cancer, potentially due to elevated ACE2 expression in these tissues [165]. The connection between ACE2 and poor outcomes in HER2-positive breast cancer, coupled with its role in SARS-CoV-2 infection, further complicates the prognosis for affected individuals.

Pancreatic cancer

Pancreatic adenocarcinoma, a highly lethal cancer, may be influenced by SARS-CoV-2's modulation of gene expression in pancreatic tissues [136]. Key genes involved in tumorigenesis, such as *PTEN*, *CREB1*, *CASP3*, and *SMAD3*, may be upregulated in response to the virus, accelerating pancreatic cancer development. Chronic inflammation driven by immune responses to SARS-CoV-2 could further facilitate oncogenesis, often allowing pancreatic cancer to progress undetected until advanced stages [166].

Colorectal cancer (CRC)

CRC development in COVID-19 patients might be linked to disturbances in the gut microbiota caused by viral interference with ACE2 function. SARS-CoV-2 induces gut dysbiosis, characterized by a loss of beneficial bacteria and an increase in pathogenic strains [138]. This dysbiosis weakens gut immunity, contributing to chronic inflammation, a known risk factor for CRC [167]. The gastrointestinal symptoms commonly observed in COVID-19, such as diarrhea and inflammation, may exacerbate CRC risk by causing persistent mucosal damage [168].

Oral cancer

Viral-induced changes in angiogenesis and extracellular matrix regulation may contribute to oral cancer. SARS-CoV-2 modulates levels of Ang-2 and extracellular matrix metalloproteinase inducer (EMMPRIN), which are key to tumor growth and metastasis [111]. Increased Ang-2 levels, driven by ACE2 downregulation, have been associated with oral cancer, suggesting a mechanism linking the infection to oral carcinogenesis [169].

Gastric cancer

Critically ill, hospitalized, and SARS-CoV-2-infected individuals exhibit a notably higher risk of gastric cancer. This may be attributed to prolonged viral replication in the gastrointestinal tract, where ACE2 and TMPRSS2 receptors are more highly expressed, enabling greater viral entry and infection [146, 170].

Head and neck cancer

Interestingly, COVID-19 patients appear to have a lower risk of head and neck cancer, which could be explained by reduced TMPRSS2 expression in these tissues [149]. This limits viral entry and minimizes cellular damage in these areas.

MR offers a powerful framework to study the causal links between SARS-CoV-2 infection and cancer [126]. The observed associations between COVID-19 severity, immune dysregulation, and cancer risk highlight the importance of understanding the long-term oncogenic effects of viral infections. Advancing our knowledge in this area could lead to the development of novel therapeutic strategies to counteract the cancer-promoting consequences of viral infections like COVID-19.

The role of viral infections in cancer development: implications of COVID-19 for long-term cancer risk

Viral infections have long been recognized as significant contributors to cancer development, with approximately 15% of all cancer cases worldwide linked to carcinogenic viruses [15]. Research exploring the relationship between viruses and cancer began in the mid-1960s, following the discovery of the first human oncogenic virus [171]. This breakthrough led to extensive investigations into how viruses contribute to tumorigenesis. Today, several viruses are strongly associated with specific cancer types, underscoring the profound impact of viral infections on cancer risk [172].

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has added new complexities to understanding the relationship between viral infections and long-term health outcomes, including potential cancer risks [105]. With increasing concerns about long COVID—where individuals experience prolonged symptoms months after the acute phase of infection—questions have arisen regarding its possible role in elevating long-term cancer risk [99].

Furthermore, the relationship between viral infections and cancer risk is complex, with significant public health implications [172]. Understanding how viral infections, such as SARS-CoV-2, contribute to cancer development is essential for developing effective interventions to mitigate this risk (Table 4).

Table 4. Viral mechanisms contributing to cancer development, with a focus on SARS-CoV-2

Mechanism	Description	Implications for cancer	Reference
Oncogenic potential of RNA viruses	RNA viruses, such as hepatitis C, produce viral proteins that disrupt cellular homeostasis, posing long-term oncogenic risks.	Persistent SARS-CoV-2 proteins may drive immune dysregulation, increasing cancer susceptibility.	[173, 174]
SARS-CoV-2 specific mechanisms	The spike protein enables viral entry, while nucleocapsid proteins facilitate replication. ACE2 receptor interactions influence tissue susceptibility.	SARS-CoV-2 may trigger cellular alterations linked to tumorigenesis, necessitating further investigation.	[77, 88, 175]
Chronic inflammation	Persistent infections induce prolonged inflammatory responses, promoting a pro-tumorigenic environment.	Post-COVID-19 inflammation may enhance cancer risk through sustained immune activation.	[100, 176–178]
Immunosuppression	Viral infections compromise immune function, fostering a tumor-permissive microenvironment.	Impaired immune surveillance facilitates tumor initiation and progression.	[179, 180]
Cellular senescence (CS)	Viral infections can induce CS, characterized by growth arrest and a senescence-associated secretory phenotype (SASP).	CS may exert dual effects, initially preventing tumors but later promoting chronic inflammation and cancer.	[181–183]
DNA modification	Viruses can introduce oncogenes, activate proto-oncogenes, or suppress tumor suppressor genes.	These genetic disruptions drive oncogenesis, underscoring the need for further molecular studies.	[184, 185]
Autophagy dysregulation	Viral proteins disrupt autophagy, leading to cellular damage accumulation and immune evasion.	Impaired autophagy fosters tumor development by promoting cell survival and immune resistance.	[186–188]

ACE2: angiotensin-converting enzyme 2; COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Mechanisms of virus-induced tumorigenesis

The mechanisms through which viruses contribute to cancer development are diverse. Chronic inflammation, immunosuppression, and DNA modification are key processes in viral oncogenesis [189]. Viruses can initiate cancer by introducing foreign oncogenes, overactivating human oncogenes, or inhibiting tumor suppressor genes [184]. Understanding these mechanisms is vital for unraveling the complex relationship between viral infections and cancer (Table 4).

In the context of long COVID, several hypotheses have emerged regarding its long-term effects, including the persistence of viral antigens and RNA, chronic inflammation, autoimmunity, dysbiosis of the microbiome, and tissue damage across multiple organs [190]. These factors may contribute to ongoing health complications that potentially elevate cancer risk.

SARS-CoV-2 and cellular mechanisms relevant to cancer

Key structural components of SARS-CoV-2 play crucial roles in viral entry and replication, further complicating health outcomes. The spike glycoprotein facilitates the virus's entry into host cells, while the nucleocapsid protein is essential for genome replication [191]. The membrane and envelope proteins contribute to virus assembly and structural integrity. Importantly, SARS-CoV-2 binds to the ACE2 receptor, found in various tissues, including the lungs, kidneys, and immune cells, which may lead to widespread effects on human health and potential cancer risks [192, 193].

One area of interest in exploring the link between COVID-19 and cancer risk is cellular senescence (CS), a process associated with aging and several diseases, including cancer [194, 195]. CS is triggered by stressors such as DNA damage and oxidative stress, which alter cell proliferation [196]. While CS can act as a tumor-suppressive mechanism, it also contributes to chronic inflammation through the senescence-associated secretory phenotype (SASP) [197]. Studies suggest that viral infections, including COVID-19, can induce CS, with SARS-CoV-2 shown to enhance SASP and promote CS in infected cells. Additionally, persistent DNA methylation changes have been observed in leukocytes following COVID-19 infection [172].

A pivotal area for exploration is the role of CS in the oncogenic potential of viral infections. Specifically, it is essential to examine how SARS-CoV-2-induced CS may contribute to cancer development [198]. Longitudinal studies should be initiated to assess CS markers, such as p16INK4a and p21CIP1, in patients

recovering from COVID-19 and other viral infections [199]. By correlating these markers with cancer incidence over time, we can better understand the long-term oncogenic risks associated with viral infections.

In addition to longitudinal studies, in vitro models of human epithelial cells infected with SARS-CoV-2 can be employed to study the induction of CS and the SASP. This approach will allow researchers to evaluate changes in cytokine profiles and cellular proliferation rates post-infection, providing insights into the mechanisms by which viral infections might facilitate cancer progression.

Chronic inflammation as a cancer risk factor and its role in tumor development

Chronic inflammation is a key mechanism linking viral infections to cancer risk. Persistent viral infections and immune evasion by tumor-associated viruses often lead to prolonged inflammatory responses that facilitate tumor development [177, 200]. Individuals recovering from COVID-19 may experience lasting inflammatory changes, increasing their susceptibility to cancer. Elevated levels of inflammatory markers and dysfunctional neutrophils have been observed in COVID-19 survivors, emphasizing the potential role of inflammation in heightening cancer risk [201, 202].

Chronic inflammation triggered by viral infections represents a critical pathway that may enhance cancer susceptibility [203, 204]. Investigating inflammatory markers associated with long COVID could provide insights into this relationship. Initiating cohort studies to track inflammatory markers such as C-reactive protein (CRP), IL-6, and TNF-α in long COVID patients compared to non-infected controls is essential. By examining the associations between elevated inflammatory markers and subsequent cancer diagnoses, we can better understand how persistent inflammation might contribute to oncogenesis.

Oncogenic potential of RNA viruses and SARS-CoV-2 persistence

RNA viruses, such as hepatitis C, are well-established contributors to cancer. These viruses often promote cancer by continuously expressing viral gene products that alter normal cellular functions [205]. Notably, recent studies have detected residual SARS-CoV-2 proteins in various tissues up to six months post-recovery, suggesting continued immune interactions that could be associated with an increased risk of cancer [206].

Animal models simulating chronic viral infections such as HCV, can also provide valuable insights [207]. These models can be utilized to assess the effects of sustained inflammation on tumor development and progression, allowing for a deeper understanding of the interplay between chronic inflammation and cancer.

Immunosuppression and cancer susceptibility

Immunosuppression is a critical factor in understanding the link between viral infections and cancer. The immune system plays a crucial role in eliminating tumor cells, and individuals with weakened immune responses are more prone to developing tumors [208, 209]. Studies show that SARS-CoV-2 can infect but not replicate in monocytes and macrophages, leading to immunoparalysis, which exacerbates COVID-19 progression [210–212]. The virus's ability to alter macrophage function—shifting them towards a tumor-promoting M2 macrophages phenotype—further highlights its potential role in cancer development.

Research on long COVID has also shown that patients exhibit distinct immunological profiles, including highly activated innate immune cells, reduced numbers of naive T and B cells, and elevated levels of type I and III interferons for up to eight months post-infection [190, 213]. SARS-CoV-2 additionally disrupts epigenetic regulation, impairing the host's ability to mount effective immune responses, which may contribute to chronic inflammation and increased cancer risk. The virus appears to evade recognition by Toll-like receptor 4 (TLR4), leading to diminished immune responses during the early stages of infection [102, 214].

A vital area of research involves examining the mechanisms through which viral infections, particularly SARS-CoV-2, cause immunosuppression and their implications for tumorigenesis [215]. Immune profiling

through the immunophenotyping of peripheral blood mononuclear cells from long COVID patients could reveal changes in immune cell populations, with specific focus on naive T and B cells. Such profiling is crucial for understanding how viral infections may alter immune surveillance mechanisms that typically protect against cancer [216].

Additionally, functional assays should be performed to assess the cytotoxic activity of immune cells co-cultured with cancer cell lines. Evaluating the functional capacity of these immune cells in the context of tumor surveillance will help identify potential deficits in immune responses that may permit tumor development.

Autophagy dysregulation and cancer development

Autophagy, a cellular process critical for maintaining homeostasis, is also disrupted by SARS-CoV-2 and other viruses. Several viral proteins interfere with autophagy, preventing its normal induction and causing the accumulation of damaged proteins and organelles, which can create a pro-cancerous environment [217, 218]. Conversely, SARS-CoV-2 can exploit autophagy to degrade major histocompatibility complex I (MHC-I), aiding immune evasion—a strategy also employed by cancer cells [219, 220].

The dysregulation of autophagy by viral proteins warrants further investigation in the context of cancer development. Biochemical assays, such as LC3-II quantification and p62 degradation analysis, should be used to measure autophagy flux in cells infected with SARS-CoV-2 [221, 222]. These assessments will provide insights into how viral infections may disrupt cellular homeostasis and potentially contribute to tumorigenesis.

Moreover, exploring pharmacological agents that enhance autophagic processes in viral-infected models could illuminate potential therapeutic strategies for mitigate cancer risk. Such interventions might restore normal autophagic function and counteract the oncogenic effects of viral infections.

COVID-19 outcomes in cancer patients—variability across cancer types and treatments

The outcomes of COVID-19 in cancer patients vary significantly based on the type of cancer and the treatments they have undergone (Table 5) [223]. While cancer patients generally face higher mortality rates from COVID-19, these data must be interpreted with caution due to variability in reporting methods. Some studies report overall mortality rates, while others focus on short-term mortality (e.g., 30-day mortality) [27]. Additionally, the strain on healthcare systems has varied across regions, complicating direct comparisons. Despite these discrepancies, the general trends indicate that cancer patients, particularly those undergoing recent or active treatments, remain at heightened risk [224, 225].

Table 5. COVID-19 outcomes in cancer patients: impact of cancer type and treatment

Category	Details	Reference
Overall COVID-19 outcomes in cancer patients	- Cancer patients face higher COVID-19 mortality, with outcomes varying by cancer type and treatment.	[27, 223, 225]
	- Studies report on both overall and short-term mortality rates.	
Impact of cancer type on COVID-19 outcomes	**Hematologic malignancies:**	[226–231]
	- Worse COVID-19 outcomes, with a 33% mortality rate in a European study.	
	Solid tumors:	
	- High risk in lung, gastrointestinal, and CNS cancers, with lung cancer patients being particularly vulnerable.	
Cancer treatment and COVID-19 outcomes	**Chemotherapy & chemoimmunotherapy:**	[232–235]
	- Increased risk of severe outcomes due to immunosuppression.	
	Immunotherapy, targeted, & endocrine therapies:	
	- Endocrine therapies linked to fewer complications.	

Table 5. COVID-19 outcomes in cancer patients: impact of cancer type and treatment (*continued*)

Category	Details	Reference
Role of recent treatments on COVID-19 outcomes	**Chemotherapy:**	[236–239]
	- Conflicting data on risk; a UK study found no increased risk, while others reported higher mortality, especially in hematologic cancers.	
	Endocrine & other therapies:	
	- Endocrine therapies are linked to fewer complications.	
COVID-19 outcomes in cancer patients: research directions	**Preventative therapeutics:**	[73, 120, 240]
	- Development of agents to counter SARS-CoV-2's oncogenic effects.	
	Cancer surveillance:	
	- Trials needed to assess long-term cancer risks in COVID-19 survivors.	
	Omics approaches:	
	- Genomic and proteomic research essential for understanding long-term oncogenic effects.	

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Impact of cancer type on COVID-19 outcomes

Hematologic malignancies

Patients with hematologic cancers, such as leukemia, face significantly worse outcomes when infected with SARS-CoV-2 [226]. Studies have consistently shown higher mortality rates in this group. For instance, a European study reported a 33% mortality rate among patients with hematologic cancers and COVID-19, emphasizing the vulnerability of these patients (Table 5) [227, 228].

Solid tumors

Among patients with solid tumors, those with lung, gastrointestinal, and central nervous system cancers are at the highest risk of severe COVID-19 [229]. Lung cancer patients, in particular, show poor outcomes due to the combined impact of underlying respiratory conditions, a history of smoking, and compromised pulmonary function. This is supported by multinational registries like the Thoracic Cancers International COVID-19 Collaboration (TERAVOLT), which noted high hospitalization and mortality rates among lung cancer patients [230, 231].

Cancer treatment and COVID-19 outcomes

Chemotherapy and chemoimmunotherapy

Patients undergoing recent systemic therapies, especially chemotherapy and chemoimmunotherapy, are at increased risk for severe COVID-19 outcomes. The immunosuppressive effects of chemotherapy likely contribute to worse outcomes in cancer patients [232, 233]. In light of this, improved risk stratification is essential to guide clinical decision-making. Healthcare systems must also allocate resources carefully to manage the higher burden imposed by this vulnerable population (Table 5).

Immunotherapy, targeted therapy, and endocrine therapy

Other cancer therapies, such as immunotherapy, targeted therapy, and endocrine therapy, exhibit more nuanced effects on COVID-19 outcomes [234]. Endocrine treatments, which are often prescribed to healthier patients, have been associated with fewer complications. In contrast, therapies like immunotherapy and targeted therapy need further investigation, as their impacts on COVID-19 outcomes are less clear.

The findings underscore the importance of tailoring cancer treatments to minimize the risk of severe COVID-19 outcomes while ensuring patients continue to receive essential care [235]. Cancer care strategies should consider both the type of cancer and the patient's overall health, including their immune status and recent treatments. This personalized approach will be critical for optimizing care during pandemics (Table 5) [241].

The role of recent treatments in COVID-19 outcomes

Chemotherapy

While some studies have reported an association between recent chemotherapy treatment and worse COVID-19 outcomes, others have not found a clear link [232]. For example, the UK Coronavirus Cancer Monitoring Project found no significant increase in risk from chemotherapy. In contrast, data from the COVID-19 and Cancer Consortium suggested that chemotherapy could elevate mortality risks, particularly in patients with hematologic malignancies (Table 5) [236, 237]. This inconsistency highlights the complexities of assessing cancer treatment risks during COVID-19 and calls for further research to clarify these relationships.

Endocrine and other therapies

Endocrine therapies are associated with fewer complications in COVID-19 outcomes. This could be attributed to the fact that endocrine treatments are often prescribed to patients with fewer comorbidities, potentially leading to a more favorable response to the virus [238, 239]. However, more research is needed to assess how therapies like immunotherapy and targeted treatments may affect COVID-19 outcomes.

Nanotechnology-based drug delivery for cancer treatment and COVID-19 management

The treatment of cancer in the presence of COVID-19 presents significant challenges, necessitating innovative therapeutic approaches. Nanotechnology-based drug delivery systems have shown great potential in enhancing cancer treatment efficacy while simultaneously addressing SARS-CoV-2 infection. The application of folate-functionalized PLGA-PEG nanoparticles (NPs) loaded with metformin (Met) has demonstrated promising anticancer effects against breast cancer cells, effectively inducing apoptosis and inhibiting tumor growth [242]. Similarly, the co-encapsulation of Artemisinin (Art) and Chrysin (Chr) in PEGylated PLGA NPs has exhibited synergistic anti-proliferative effects on cancer cells [243]. These nanocarriers not only improve drug bioavailability and targeted delivery, but they also offer a potential dual therapeutic strategy. This strategy provides anticancer benefits while mitigating the complications associated with COVID-19 in cancer patients. Given the increased vulnerability of cancer patients to viral infections, integrating nanotechnology into treatment regimens could optimize therapeutic outcomes, enhancing both cancer therapy and viral infection management.

Future research directions in preventative therapies, cancer surveillance and omics for COVID-19 survivors

Development of preventative therapeutics

The development of therapeutics to mitigate the oncogenic effects of SARS-CoV-2 or modulate inflammatory responses offers an exciting avenue for research [73]. Such agents could help reduce cancer risks in patients recovering from COVID-19 and improve their overall health outcomes.

Cancer surveillance in COVID-19 survivors

Establishing clinical trials focused on cancer surveillance in patients with a history of SARS-CoV-2 infection is crucial [240]. By monitoring these patients for early signs of specific cancers, researchers can better understand the long-term implications of COVID-19 and provide early intervention strategies (Table 5).

Integrating omics approaches

Integrative omics approaches (genetic, transcriptomic, proteomic, and metabolomic analyses) are essential for understanding the long-term health impacts of COVID-19 on cancer patients [120, 244]. These approaches can uncover novel biomarkers and pathways, facilitating a better understanding of the virus's potential oncogenic effects.

While cancer patients face higher mortality rates from COVID-19, there is still much to learn about the complex interplay between cancer types, treatments, and COVID-19 outcomes. Ongoing research into the molecular mechanisms, treatment-related risks, and long-term health impacts of SARS-CoV-2 will be essential in developing evidence-based strategies to manage cancer care after the pandemic (Table 5).

Organizing future research on cancer care during global crises: addressing healthcare disruptions, treatment delays, and long COVID

The COVID-19 pandemic has highlighted vulnerabilities in global healthcare systems, particularly in cancer care. It has disrupted cancer treatments, delayed early detection, and impeded preventive measures, leading to lasting impacts on patient outcomes [41]. Looking ahead, research must focus on strategies to ensure the resilience of cancer care systems during global crises (Figure 1). Several key research areas focused on mitigating the long-term effects of healthcare disruptions, improving treatment accessibility, and addressing the challenges posed by long COVID in cancer patients are outlined below and in Figure 1.

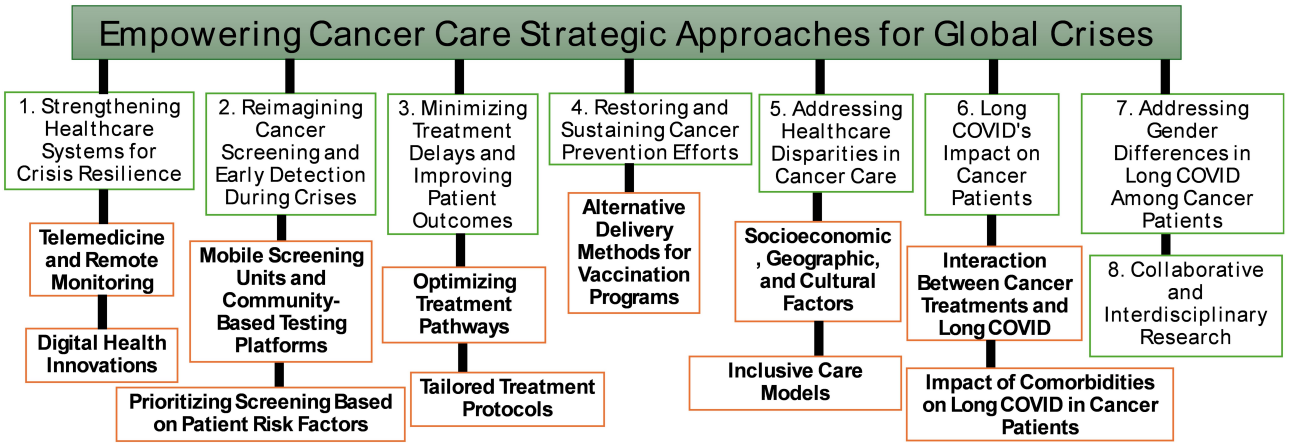

Figure 1. Key research areas in response to the challenges posed by the COVID-19 pandemic on cancer care. COVID-19: coronavirus disease 2019

Strengthening healthcare systems for crisis resilience

A fundamental aspect of preparing for future global crises is to build healthcare systems that can withstand and adapt to sudden disruptions [245]. Research should aim to identify and implement strategies that ensure continuity in essential services, such as cancer screening and treatment. Key areas of research include:

a. Telemedicine and remote monitoring: Telemedicine, remote monitoring, and digital health tools have proven invaluable in maintaining access to healthcare during the pandemic [246]. These technologies can play a crucial role in cancer care during future emergencies. Research should explore the effectiveness of these tools for cancer patients, particularly those at high risk of complications from delayed care. For example, telehealth platforms can facilitate consultations, monitoring of symptoms, and follow-up care, ensuring that cancer patients continue to receive timely medical attention during crises [247].

b. Digital health innovations: Beyond remote consultations, research should focus on digital health innovations, such as wearable devices that monitor vital signs or artificial intelligence (AI)-based tools that assist in the diagnosis and treatment of cancer. These tools can help provide continuous care even when traditional healthcare facilities are overwhelmed, thus ensuring that cancer patients remain connected to their healthcare providers and receive timely assessments [248, 249].

Reimagining cancer screening and early detection during crises

During periods of healthcare strain, it is critical to reimagine how cancer screening is conducted to ensure early detection and timely intervention. Research should focus on developing new, adaptable screening methods that can be deployed during emergencies, with a focus on:

a. Mobile screening units and community-based testing platforms: Innovative approaches like mobile screening units or community-based testing platforms can be rapidly mobilized during crises [250].

Research should explore the logistical feasibility, accessibility, and accuracy of these methods, ensuring they reach diverse populations, including those in remote or underserved areas.

b. Prioritizing screening based on patient risk factors: During periods of crisis, not all cancer screenings can be performed on the same scale as during normal times. Research should focus on how to prioritize screenings based on individual patient risk factors. This will ensure that the most vulnerable populations, such as those with a family history of cancer or other risk factors, receive timely care. This strategy could help mitigate the impact of missed diagnoses and reduce treatment delays.

Minimizing treatment delays and improving patient outcomes

The impact of treatment delays on cancer progression and mortality is well-established, highlighting the need for future research to prioritize strategies that minimize such delays during crises. Key areas for investigation include:

a. Optimizing treatment pathways: Research should focus on streamlining diagnostic procedures and treatment protocols to reduce the time to intervention [251]. This could involve implementing triage systems to prioritize high-risk cancer cases and evaluating the feasibility of expediting treatments such as adjuvant chemotherapy. By optimizing treatment pathways, healthcare systems can better manage patient care during times of crisis and reduce the risk of worsened outcomes.

b. Tailored treatment protocols: Some cancer types may be more vulnerable to the effects of delayed care than others [241, 252]. Research should investigate whether treatment protocols can be adjusted for specific cancer types to mitigate risks during healthcare disruptions. For instance, studies could examine whether certain treatments can be adjusted or delivered more quickly without compromising patient safety or treatment efficacy.

Restoring and sustaining cancer prevention efforts

Global crises like the COVID-19 pandemic have disrupted critical cancer prevention programs, such as vaccinations for HPV [253]. These disruptions can lead to an increase in preventable cancers, particularly those linked to viral infections. To ensure continued cancer prevention efforts during emergencies, future research should explore:

a. Alternative delivery methods for vaccination programs: Research should explore alternative methods of delivering cancer prevention vaccines during crises. For example, school-based or community-wide vaccination initiatives could be developed to ensure that vaccination coverage is maintained even when traditional healthcare settings are compromised [254]. These models would make vaccines more accessible and help maintain high vaccination rates during emergencies.

b. Long-term impact of disrupted vaccination schedules: Studies should assess the long-term effects of disrupted vaccination schedules, particularly regarding the risk of cancer in populations that miss doses or are delayed in receiving critical vaccines [255]. Understanding these effects will help in developing strategies to recover from gaps in vaccination coverage and to prevent future cancer cases that might have been avoidable.

Addressing healthcare disparities in cancer care

The COVID-19 pandemic has exacerbated existing healthcare disparities, particularly among underserved populations, making access to timely cancer care even more challenging [225, 256]. Research must identify and address the systemic barriers that contribute to unequal access and treatment delays. Key areas of focus include:

a. Socioeconomic, geographic, and cultural factors: Research should investigate how socioeconomic, geographic, and cultural factors contribute to unequal access to cancer care. Understanding these

factors will help identify the populations most at risk of being disproportionately affected by delays in cancer care and treatment during a global crisis [257].

b. Inclusive care models: Targeted interventions, such as community-specific outreach programs and pilot models of inclusive care, should be developed to reduce inequities in cancer care [258]. These programs can ensure that vulnerable populations, particularly those in remote or underserved areas, are not left behind during crises and receive the care they need.

Long COVID and its impact on cancer patients

The COVID-19 pandemic has resulted in persistent health complications, collectively termed long COVID, which pose significant challenges for vulnerable populations, including cancer patients. Given their compromised immune systems and the physiological strain imposed by oncological treatments, cancer patients may experience heightened susceptibility to the prolonged effects of COVID-19 [259]. Understanding the interplay between long COVID and cancer is essential for developing effective clinical management strategies.

A critical area of investigation involves the interaction between cancer treatments and long COVID. Therapies such as chemotherapy, radiotherapy, and immunotherapy exert profound immunomodulatory effects, which could either exacerbate or mitigate long COVID symptoms [202, 260]. Chemotherapy, by suppressing immune function, may prolong viral persistence, delay viral clearance, and exacerbate systemic inflammation, thereby intensifying long COVID symptoms such as fatigue, cognitive impairment, and organ dysfunction [232]. Additionally, chemotherapy-induced lymphopenia could increase susceptibility to secondary infections, further complicating recovery from long COVID [261]. Radiotherapy, particularly in patients with thoracic malignancies, can cause pulmonary fibrosis and chronic lung injury, potentially compounding respiratory complications associated with long COVID [262]. The impact of immunotherapy, including immune checkpoint inhibitors, on long COVID remains complex. While these agents enhance anti-tumor immunity, they may also contribute to hyperinflammatory states, increasing the risk of autoimmune-like manifestations of long COVID [263]. Furthermore, corticosteroids, commonly used in oncology to manage treatment-related adverse effects, may suppress immune responses to COVID-19 [264], leading to prolonged viral shedding and delayed resolution of symptoms.

Additionally, the presence of comorbidities—including hypertension, diabetes, and cardiovascular disease—compounds the complexity of long COVID in cancer patients. These conditions not only influence acute and post-acute COVID-19 outcomes but may also alter the trajectory of recovery in oncological populations [265, 266]. Chronic systemic inflammation, a hallmark of both long COVID and cancer, may create a tumor-promoting microenvironment by sustaining elevated levels of pro-inflammatory cytokines such as IL-6, TNF-α, and CRP [267]. These inflammatory mediators can contribute to immune evasion, tumor growth, and metastasis, thereby accelerating cancer progression in affected patients. Moreover, endothelial dysfunction and microvascular damage observed in long COVID may impair tissue oxygenation and nutrient supply to tumors, potentially influencing treatment responses and disease progression [268]. Long COVID-associated metabolic disturbances, such as insulin resistance and mitochondrial dysfunction, could exacerbate cancer-associated cachexia, reduce treatment tolerance, and negatively impact overall survival [269]. Identifying predictive biomarkers, such as circulating inflammatory markers or metabolic signatures, could help stratify cancer patients at the highest risk for adverse long COVID outcomes, enabling more targeted and individualized therapeutic approaches.

Future research should prioritize a comprehensive assessment of these factors to inform evidence-based strategies for mitigating long COVID's impact on cancer patients. A multidisciplinary approach incorporating oncology, immunology, infectious diseases, and precision medicine will be essential in developing targeted interventions. Clinical trials should investigate the long-term impact of COVID-19 on cancer progression, treatment efficacy, and patient survival, particularly in the context of novel immunotherapies and emerging antiviral treatments. Additionally, prospective cohort studies should explore whether specific cancer subtypes or treatment regimens predispose patients to more severe or prolonged manifestations of long COVID.

Addressing gender differences in long COVID among cancer patients

There is emerging evidence that gender-based differences in immune response and hormonal fluctuations may influence the prevalence and severity of long COVID symptoms, particularly among female cancer patients [270]. Research should explore how these gender differences contribute to the higher incidence of symptoms such as fatigue and sleep disturbances in women. Understanding these differences, alongside the effects of cancer treatments, could lead to more personalized and effective management strategies for long COVID in female cancer patients.

Collaborative and interdisciplinary research

Addressing the complex interplay between cancer care, long COVID, and healthcare disruption requires the formation of interdisciplinary research teams. These teams should bring together expertise from oncology, virology, immunology, neurobiology, and other relevant fields to develop targeted interventions for cancer patients affected by long COVID [1, 271]. Such collaborative efforts will address the immediate challenges faced by cancer patients during times of crisis. They will also provide valuable insights into enhancing the resilience of cancer care systems, particularly in maintaining continuity of care during public health emergencies.

The impact of global crises, such as the COVID-19 pandemic, has underscored the urgent need for comprehensive research into cancer care during periods of disruption [41]. This research must address both the direct and indirect effects of global health crises on cancer patients. It should include disruptions in diagnosis, treatment delays, and the psychological and social impacts of these crises. Future research should prioritize strengthening healthcare system resilience and reimagining cancer screening protocols to adapt to evolving risks. It should also focus on minimizing treatment delays through innovative solutions, restoring prevention efforts that may have been sidelined during crises, addressing healthcare disparities, and understanding the specific impacts of long COVID on cancer treatment outcomes [44, 272]. In this context, global health organizations could play a critical role in developing international frameworks for preparedness. Their efforts could focus on building rapid response capabilities to address cancer care disruptions during emergencies. Additionally, they should ensure equitable access to cancer treatment across diverse populations and foster global collaboration among researchers, healthcare professionals, and policymakers.

Specific recommendations for future preparedness should include the establishment of global databases to monitor cancer patient outcomes during public health crises [273]. This would facilitate data-sharing across borders, helping them to better understand the challenges faced by cancer patients in different regions. Additionally, creating scalable telemedicine platforms to ensure continued access to cancer care remotely, especially in resource-limited settings, will be crucial [274]. Telemedicine can also facilitate remote consultations and follow-up care, alleviating the burden on healthcare facilities during high-demand periods. Another key recommendation is the development of flexible healthcare policies that allow for rapid adaptation in times of emergency. These policies should include adjusting cancer screening protocols, treatment regimens, and prevention efforts based on real-time data and emerging evidence [275].

Through these initiatives, we can ensure that cancer care remains robust and accessible, even in the face of future emergencies. Ultimately, this will safeguard vulnerable populations, improve patient outcomes, and fortify healthcare systems to be more resilient against future global challenges.

Real-world policy implementations and lessons from past pandemic responses

The COVID-19 pandemic and previous public health crises have underscored the critical role of policy in sustaining resilient cancer care systems [56, 273]. Effective policymaking ensures that disruptions to oncology treatment are minimized, healthcare infrastructure is reinforced, and equitable access to care is maintained even in times of crisis. By analyzing past interventions, we can identify key strategies for strengthening cancer care in future emergencies.

Government-led healthcare adaptations

In response to the pandemic, governments worldwide implemented emergency measures, including expedited telehealth approvals, regulatory flexibility for cancer treatments, and financial support for affected patients [276]. While these adaptations helped mitigate immediate challenges, their long-term effectiveness and integration into routine care remain key areas for evaluation.

Public-private partnerships in crisis response

Collaboration between governments, pharmaceutical companies, healthcare providers, and research institutions played a crucial role in sustaining cancer care during the pandemic [277]. These partnerships facilitated the rapid development of treatments, stabilized supply chains, and introduced innovative care delivery models [278]. Moving forward, policy efforts should focus on optimizing these collaborations through streamlined clinical trials, improved data-sharing frameworks, and mechanisms that ensure equitable access to oncology therapeutics. Analyzing successful and unsuccessful partnerships can provide valuable insights into improving coordination and efficiency in future health crises.

Policy strategies for equitable access

The pandemic exacerbated existing healthcare disparities, disproportionately affecting vulnerable populations. Examining national and global policies on healthcare equity can help inform more inclusive approaches to oncology care [279, 280]. Key areas of focus include evaluating the effectiveness of subsidized treatment programs, flexible insurance policies, and community-based outreach initiatives. Additionally, research into alternative care delivery models and resource allocation strategies can help ensure that equitable access to cancer treatment [257] remains a priority during future crises.

By integrating lessons from past public health responses, policymakers can develop evidence-based strategies to strengthen cancer care systems. A forward-thinking approach—centered on adaptability, collaboration, and inclusivity—will be essential in ensuring uninterrupted oncology services in the face of future global health challenges.

Temporal epidemiological association between the COVID-19 pandemic and the increase in cancer incidence

The COVID-19 pandemic has profoundly impacted global health systems, not only through the direct effects of the virus but also by disrupting essential healthcare services, including cancer prevention, diagnosis, and treatment [1, 2]. Recent epidemiological data suggest a temporal association between the pandemic and an increase in cancer incidence across various regions, with this association being multifactorial (Figure 2). Factors such as delays in screening, interruptions in treatment, and reduced access to healthcare services have all contributed to this rise.

A key factor driving the increase in cancer incidence is the delay in diagnoses resulting from the strain placed on healthcare systems. As hospitals became overwhelmed with COVID-19 patients, many elective medical procedures, including routine cancer screenings, were postponed or canceled. This was observed across several countries, including the United States, Italy, Spain, and the United Kingdom, where screening programs for breast, colorectal, and cervical cancers experienced significant declines during the early phases of the pandemic [3–5]. For example, a dramatic drop in cancer screenings was reported in the United States in 2020, with CRC screenings decreasing by more than 80% in some states [6]. This delay in diagnosis led to the identification of cancers at more advanced stages, contributing to higher incidence rates in the years following the pandemic.

Patient behavior also played a crucial role in the observed temporal association. Fear of contracting COVID-19 in healthcare settings caused many individuals to avoid medical consultations and screenings, particularly in regions with high COVID-19 mortality rates [7]. In countries like Brazil and India, where healthcare systems were significantly strained by the pandemic, the number of cancer diagnoses initially fell. However, the postponement of treatments and failure to diagnose cancers early likely resulted in a rise

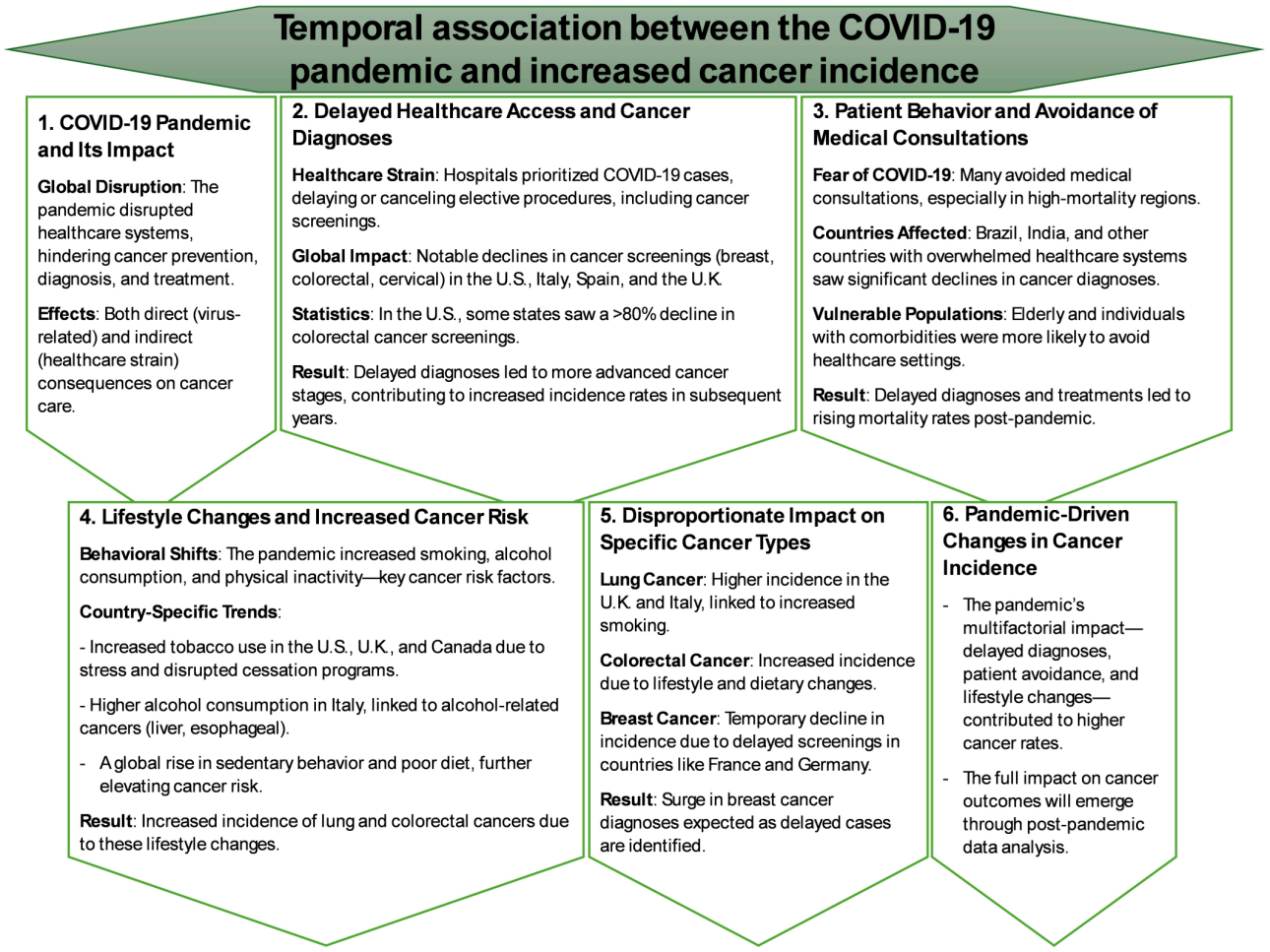

Figure 2. Temporal association between the COVID-19 pandemic and increased cancer incidence. COVID-19: coronavirus disease 2019

in mortality rates in the years that followed [8, 9]. Vulnerable populations, such as the elderly and individuals with preexisting comorbidities, were particularly affected, as they are at higher risk for certain cancers. As a result, delays in diagnosis and treatment were compounded, and the full impact on cancer incidence may not be fully understood until comprehensive post-pandemic data is available.

The pandemic has also been associated with significant changes in lifestyle behaviors, such as increased smoking, alcohol consumption, and physical inactivity, all of which are well-established risk factors for several types of cancer [10, 11]. Studies conducted in countries like the United States, the United Kingdom, and Canada have shown an increase in tobacco use during the pandemic, likely due to heightened stress and the closure of smoking cessation programs [12, 13]. Additionally, disruptions in dietary habits, increased sedentary behavior, and reduced physical activity were observed worldwide, further contributing to an increased cancer risk. For example, the incidence of lung and CRCs during the pandemic may reflect the compounded effects of these lifestyle changes [14, 15]. In Italy, for instance, a sharp rise in alcohol consumption in 2020 has been linked to an increase in alcohol-related cancers, such as liver and esophageal cancers.

Certain types of cancer appear to have been disproportionately impacted by the COVID-19 pandemic. In countries such as the United Kingdom and Italy, the incidence of lung cancer—strongly associated with smoking—and CRC, linked to dietary and lifestyle factors, increased in the years following the onset of the pandemic [16, 17]. On the other hand, some cancer types, particularly those reliant on early detection programs such as breast cancer, experienced a temporary decline in incidence due to postponed screenings [18, 19]. However, an anticipated surge in diagnoses is expected in the future, as delayed cases are detected. In countries like France and Germany, for example, breast cancer diagnoses sharply fell in 2020, but these declines are expected to reverse as delayed diagnoses are made in the years ahead [20, 21].

Discussion, conclusions, and future directions

The interplay between cancer and COVID-19 has revealed significant challenges, particularly for immunocompromised patients who face increased risks from both acute infection and long-term complications [72, 281]. The pandemic has exacerbated vulnerabilities in cancer care, disrupting treatments and delaying diagnoses, thereby contributing to poorer outcomes [41]. These challenges underscore the urgent need to understand the mechanisms through which SARS-CoV-2 may influence cancer progression and to develop robust mitigation strategies tailored to protect this high-risk group. Additionally, the long-term health consequences of COVID-19, including the emerging phenomenon of long COVID, highlight the necessity of sustained monitoring and comprehensive healthcare planning for cancer patients during and after pandemics [66, 282]. Future research should focus on identifying personalized intervention strategies to mitigate the long-term consequences of SARS-CoV-2 in oncology settings, ensuring that affected individuals receive continuous and adaptive care.

Addressing the unique vulnerabilities of cancer patients requires a multifaceted approach that integrates vaccination, timely treatment, and ongoing support for individuals experiencing persistent symptoms [283, 284]. Given the potential oncogenic risks associated with SARS-CoV-2, continued research into its long-term effects on cancer patients is essential. Such research will not only enhance our understanding of COVID-19's broader health impacts but will also inform future public health strategies, ensuring that cancer patients receive appropriate protection and care during future pandemics. Effective data collection, alongside the refinement of clinical guidelines, will be crucial for improving patient outcomes and strengthening healthcare system preparedness. Furthermore, integrating AI and machine learning models to predict cancer risk in post-COVID-19 patients could provide valuable insights into early detection and preventive strategies.

A growing body of research investigating the role of viral infections in cancer development underscores the significance of viruses, such as SARS-CoV-2, in modulating long-term health risks, including cancer susceptibility [91, 285]. While traditional oncogenic viruses, such as HPV and HBV, have well-established links to cancer, emerging evidence suggests that SARS-CoV-2 may also exhibit oncogenic potential. This may occur through mechanisms such as chronic inflammation, CS, immune dysregulation, and autophagy disruption [88, 156]. These findings raise critical concerns regarding the potential for SARS-CoV-2 to increase cancer risk, particularly as long COVID becomes an area of significant clinical focus. However, the precise molecular pathways linking COVID-19 to oncogenesis remain poorly understood, necessitating further investigation into the cellular and molecular consequences of SARS-CoV-2 infection. Exploring the interactions between viral proteins and key oncogenic pathways, such as the p53 and PI3K-AKT signaling axes, will be essential for elucidating the mechanistic basis of SARS-CoV-2-driven tumorigenesis.

Longitudinal studies are essential to clarify the relationship between COVID-19 and cancer risk, with an emphasis on monitoring immune responses, inflammatory markers, and cellular stress in recovered patients. Investigating mechanisms such as CS, chronic inflammation, and immunosuppression will provide valuable insights into how SARS-CoV-2 may alter tumor-suppressive pathways, potentially fostering an environment conducive to cancer development [177]. Additionally, MR studies can help identify populations with a genetic predisposition to increased cancer risk following SARS-CoV-2 infection [126]. As the world continues to navigate the pandemic's aftermath, the potential long-term oncogenic risks posed by COVID-19 highlight the need for interdisciplinary research to inform preventive strategies and therapeutic interventions aimed at mitigating future cancer incidences linked to viral infections. Future efforts should include large-scale biobanking and genome-wide association studies (GWAS) to uncover genetic susceptibilities that may predispose individuals to post-COVID-19 malignancies, facilitating early intervention measures.

The molecular impact of SARS-CoV-2 on cancer development presents a complex and multifaceted challenge. The virus has been implicated in dysregulating key cellular pathways, such as the RAAS and epigenetic mechanisms, both of which are recognized contributors to oncogenesis [286]. SARS-CoV-2's

interactions with tumor suppressors and oncogenes, as well as its role in promoting inflammation and oxidative stress, align with established cancer-promoting mechanisms [287]. However, definitive evidence directly linking SARS-CoV-2 to tumorigenesis remains elusive. Continued exploration of virus-encoded circRNAs, inflammatory cytokines, and viral proteins is critical for understanding their impact on cancer-related gene networks and for developing novel therapeutic strategies to mitigate the potential oncogenic effects of COVID-19 [81, 104]. Additionally, single-cell transcriptomics and spatial proteomics could provide unprecedented insights into how SARS-CoV-2 reshapes the tumor microenvironment, potentially driving malignancies in predisposed individuals.

Future research should prioritize investigating the long-term oncogenic potential of SARS-CoV-2, particularly in cancer survivors and individuals with a history of chronic infection. Comparative studies examining SARS-CoV-2's oncogenic mechanisms alongside those of established oncogenic viruses will be valuable in identifying shared and unique pathways. Integrative omics approaches, coupled with mechanistic studies of viral protein function, will aid in the identification of biomarkers and pathways relevant to both cancer progression and prevention [288, 289]. Additionally, research into SARS-CoV-2-induced epigenetic changes and molecular interactions between viral proteins and host cell factors will be pivotal in unveiling the full spectrum of its influence on cancer development [102]. This research will ultimately guide personalized care and cancer surveillance strategies. Developing predictive models based on multi-omics data will be crucial for stratifying patients at higher risk for post-viral malignancies and tailoring precision oncology approaches.

Ensuring the continuity and resilience of cancer care during global crises is paramount, as demonstrated by the widespread disruptions experienced during the COVID-19 pandemic [273]. Future research must prioritize strategies that mitigate healthcare interruptions, improve access to screenings and treatments, and address the unique challenges cancer patients face in the context of long COVID. Advancing telemedicine, developing adaptable screening methods, and leveraging digital health innovations will help sustain essential services during crises [290]. Furthermore, targeted efforts to reduce healthcare disparities and explore the long-term effects of COVID-19 on cancer patients are crucial to improving patient outcomes [291]. By integrating real-time epidemiological surveillance with AI-driven predictive modeling, healthcare systems can proactively identify emerging risks and implement timely interventions. Establishing an international research consortia focused on post-viral oncology will be instrumental in accelerating discoveries and translating findings into clinical practice, ensuring a more resilient and equitable healthcare future.

Abbreviations

ACE2: angiotensin-converting enzyme 2

AI: artificial intelligence

Ang-2: angiopoietin-2

circRNAs: circular RNAs

COVID-19: coronavirus disease 2019

CRC: colorectal cancer

CS: cellular senescence

EMMPRIN: extracellular matrix metalloproteinase inducer

EMT: epithelial-mesenchymal transition

HPV: human papillomavirus

miRNAs: microRNAs

MR: Mendelian randomization

pRB: protein retinoblastoma

RAAS: renin-angiotensin-aldosterone system

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

SASP: senescence-associated secretory phenotype

Declarations

Author contributions

MMN and OAA equally contributed to: Conceptualization, Writing—original draft, Writing—review & editing.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Publisher's note

References

1. Tsamakis K, Gavriatopoulou M, Schizas D, Stravodimou A, Mougkou A, Tsiptsios D, et al. Oncology during the COVID-19 pandemic: challenges, dilemmas and the psychosocial impact on cancer patients. Oncol Lett. 2020;20:441–7. [DOI] [PubMed] [PMC]
2. Bashkin O, Nahmias R, Attar S, Moshe R, Asna N. Perspectives of cancer patients during the COVID-19 outbreak in Israel: The long-term implications on support and well-being in an exploratory qualitative study. Eur J Cancer Care (Engl). 2022;31:e13657. [DOI] [PubMed] [PMC]
3. Johannesen TB, Smeland S, Aaserud S, Buanes EA, Skog A, Ursin G, et al. COVID-19 in Cancer Patients, Risk Factors for Disease and Adverse Outcome, a Population-Based Study From Norway. Front Oncol. 2021;11:652535. [DOI] [PubMed] [PMC]
4. Pathania AS, Prathipati P, Abdul BA, Chava S, Katta SS, Gupta SC, et al. COVID-19 and Cancer Comorbidity: Therapeutic Opportunities and Challenges. Theranostics. 2021;11:731–53. [DOI] [PubMed] [PMC]

5. Pfortmueller CA, Spinetti T, Urman RD, Luedi MM, Schefold JC. COVID-19-associated acute respiratory distress syndrome (CARDS): Current knowledge on pathophysiology and ICU treatment - A narrative review. Best Pract Res Clin Anaesthesiol. 2021;35:351–68. [DOI] [PubMed] [PMC]
6. Zheng J, Miao J, Guo R, Guo J, Fan Z, Kong X, et al. Mechanism of COVID-19 Causing ARDS: Exploring the Possibility of Preventing and Treating SARS-CoV-2. Front Cell Infect Microbiol. 2022;12:931061. [DOI] [PubMed] [PMC]
7. Naffaa MM, Al-Ewaidat OA. Stroke risks in patients with COVID-19: multiple mechanisms of SARS-CoV-2, impact of sex and age, vaccination, and long-term infection. Dis Med. 2024;1:51. [DOI]
8. Siegler JE, Abdalkader M, Michel P, Nguyen TN. Therapeutic Trends of Cerebrovascular Disease during the COVID-19 Pandemic and Future Perspectives. J Stroke. 2022;24:179–88. [DOI] [PubMed] [PMC]
9. Corso CR, Mulinari Turin de Oliveira N, Maria-Ferreira D. Susceptibility to SARS-CoV-2 infection in patients undergoing chemotherapy and radiation therapy. J Infect Public Health. 2021;14:766–71. [DOI] [PubMed] [PMC]
10. Elkrief A, Wu JT, Jani C, Enriquez KT, Glover M, Shah MR, et al. Learning through a Pandemic: The Current State of Knowledge on COVID-19 and Cancer. Cancer Discov. 2022;12:303–30. [DOI] [PubMed] [PMC]
11. Ali JK, Riches JC. The Impact of the COVID-19 Pandemic on Oncology Care and Clinical Trials. Cancers (Basel). 2021;13:5924. [DOI] [PubMed] [PMC]
12. Howlader N, Chen HS, Noone AM, Miller D, Byrne J, Negoita S, et al. Impact of COVID-19 on 2021 cancer incidence rates and potential rebound from 2020 decline. J Natl Cancer Inst. 2025;117: 507–10. [DOI] [PubMed] [PMC]
13. Hall VG, Teh BW. COVID-19 Vaccination in Patients With Cancer and Patients Receiving HSCT or CAR-T Therapy: Immune Response, Real-World Effectiveness, and Implications for the Future. J Infect Dis. 2023;228:S55–69. [DOI] [PubMed] [PMC]
14. Bouza E, Martín Jiménez M, Alemany L, Arribas J, Bañares R, Barragán MB, et al. Overview of virus and cancer relationships. Position paper. Rev Esp Quimioter. 2021;34:525–55. [DOI] [PubMed] [PMC]
15. McLaughlin-Drubin ME, Munger K. Viruses associated with human cancer. Biochim Biophys Acta. 2008;1782:127–50. [DOI] [PubMed] [PMC]
16. White MK, Pagano JS, Khalili K. Viruses and human cancers: a long road of discovery of molecular paradigms. Clin Microbiol Rev. 2014;27:463–81. [DOI] [PubMed] [PMC]
17. Goyal R, Gautam RK, Chopra H, Dubey AK, Singla RK, Rayan RA, et al. Comparative highlights on MERS-CoV, SARS-CoV-1, SARS-CoV-2, and NEO-CoV. EXCLI J. 2022;21:1245–72. [DOI] [PubMed] [PMC]
18. Cai Z, Lu C, He J, Liu L, Zou Y, Zhang Z, et al. Identification and characterization of circRNAs encoded by MERS-CoV, SARS-CoV-1 and SARS-CoV-2. Brief Bioinform. 2021;22:1297–308. [DOI] [PubMed] [PMC]
19. Sherif ZA, Gomez CR, Connors TJ, Henrich TJ, Reeves WB; RECOVER Mechanistic Pathway Task Force. Pathogenic mechanisms of post-acute sequelae of SARS-CoV-2 infection (PASC). Elife. 2023; 12:e86002. [DOI] [PubMed] [PMC]
20. Davitt E, Davitt C, Mazer MB, Areti SS, Hotchkiss RS, Remy KE. COVID-19 disease and immune dysregulation. Best Pract Res Clin Haematol. 2022;35:101401. [DOI] [PubMed] [PMC]
21. Jafarzadeh A, Gosain R, Mortazavi SMJ, Nemati M, Jafarzadeh S, Ghaderi A. SARS-CoV-2 Infection: A Possible Risk Factor for Incidence and Recurrence of Cancers. Int J Hematol Oncol Stem Cell Res. 2022;16:117–27. [DOI] [PubMed] [PMC]
22. Chavez-MacGregor M, Lei X, Zhao H, Scheet P, Giordano SH. Evaluation of COVID-19 Mortality and Adverse Outcomes in US Patients With or Without Cancer. JAMA Oncol. 2022;8:69–78. [DOI] [PubMed] [PMC]

23. Bernard A, Cottenet J, Bonniaud P, Piroth L, Arveux P, Tubert-Bitter P, et al. Comparison of Cancer Patients to Non-Cancer Patients among COVID-19 Inpatients at a National Level. Cancers (Basel). 2021;13:1436. [DOI] [PubMed] [PMC]
24. Zhang JJ, Dong X, Liu GH, Gao YD. Risk and Protective Factors for COVID-19 Morbidity, Severity, and Mortality. Clin Rev Allergy Immunol. 2023;64:90–107. [DOI] [PubMed] [PMC]
25. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020;371:m4087. [DOI] [PubMed] [PMC]
26. Wells CR, Galvani AP. Impact of the COVID-19 pandemic on cancer incidence and mortality. Lancet Public Health. 2022;7:e490–1. [DOI] [PubMed] [PMC]
27. Erdal GS, Polat O, Erdem GU, Korkusuz R, Hindilerden F, Yilmaz M, et al. The mortality rate of COVID-19 was high in cancer patients: a retrospective single-center study. Int J Clin Oncol. 2021;26:826–34. [DOI] [PubMed] [PMC]
28. Abuhelwa Z, Alsughayer A, Abuhelwa AY, Beran A, Sayeh W, Khokher W, et al. In-Hospital Mortality and Morbidity in Cancer Patients with COVID-19: A Nationwide Analysis from the United States. Cancers (Basel). 2022;15:222. [DOI] [PubMed] [PMC]
29. Zhao L, Fu L, He Y, Li H, Song Y, Liu S. Effectiveness and Safety of COVID-19 Vaccination in Patients with Malignant Disease. Vaccines (Basel). 2023;11:486. [DOI] [PubMed] [PMC]
30. Turtle L, Elliot S, Drake TM, Thorpe M, Khoury EG, Greenhalf W, et al.; ISARIC4C Investigators. Changes in hospital mortality in patients with cancer during the COVID-19 pandemic (ISARIC-CCP-UK): a prospective, multicentre cohort study. Lancet Oncol. 2024;25:636–48. [DOI] [PubMed]
31. Le Borgne P, Feuillassier L, Schenck M, Herbrecht JE, Janssen-Langenstein R, Simand C, et al. Comparison of Short- and Long-Term Mortality in Patients with or without Cancer Admitted to the ICU for Septic Shock: A Retrospective Observational Study. Cancers (Basel). 2022;14:3196. [DOI] [PubMed] [PMC]
32. Nadkarni AR, Vijayakumaran SC, Gupta S, Divatia JV. Mortality in Cancer Patients With COVID-19 Who Are Admitted to an ICU or Who Have Severe COVID-19: A Systematic Review and Meta-Analysis. JCO Glob Oncol. 2021;7:1286–305. [DOI] [PubMed] [PMC]
33. Dagher H, Chaftari AM, Subbiah IM, Malek AE, Jiang Y, Lamie P, et al. Long COVID in cancer patients: preponderance of symptoms in majority of patients over long time period. Elife. 2023;12:e81182. [DOI] [PubMed] [PMC]
34. Bai F, Tomasoni D, Falcinella C, Barbanotti D, Castoldi R, Mulè G, et al. Female gender is associated with long COVID syndrome: a prospective cohort study. Clin Microbiol Infect. 2022;28:611.e9–16. [DOI] [PubMed] [PMC]
35. Socia D, Larie D, Feuerwerker S, An G, Cockrell C. Prediction of Long COVID Based on Severity of Initial COVID-19 Infection: Differences in predictive feature sets between hospitalized versus non-hospitalized index infections. medRxiv [Preprint]. 2023 [cited 2023 Jan 20]. Available from: https://www.medrxiv.org/content/10.1101/2023.01.16.23284634v2
36. Jaiswal A, Shrivastav S, Kushwaha HR, Chaturvedi R, Singh RP. Oncogenic potential of SARS-CoV-2-targeting hallmarks of cancer pathways. Cell Commun Signal. 2024;22:447. [DOI] [PubMed] [PMC]
37. Sun L, Surya S, Le AN, Desai H, Doucette A, Gabriel P, et al. Rates of COVID-19-Related Outcomes in Cancer Compared With Noncancer Patients. JNCI Cancer Spectr. 2021;5:Pkaa120. [DOI] [PubMed] [PMC]
38. Hansen CL, Viboud C, Simonsen L. Disentangling the relationship between cancer mortality and COVID-19 in the US. Elife. 2024;13:RP93758. [DOI] [PubMed] [PMC]
39. Challa SR, Oskrochi G, Singh GP, Chirumamilla LG, Shayegh N, Nair VK, et al. Predictors of mortality in hospitalized African American COVID-19 patients with cancer. Transl Cancer Res. 2024;13:1314–22. [DOI] [PubMed] [PMC]

40. Rüthrich MM, Giessen-Jung C, Borgmann S, Classen AY, Dolff S, Grüner B, et al.; LEOSS Study Group. COVID-19 in cancer patients: clinical characteristics and outcome-an analysis of the LEOSS registry. Ann Hematol. 2021;100:383–93. [DOI] [PubMed] [PMC]
41. Richards M, Anderson M, Carter P, Ebert BL, Mossialos E. The impact of the COVID-19 pandemic on cancer care. Nat Cancer. 2020;1:565–7. [DOI] [PubMed] [PMC]
42. Patt D, Gordan L, Diaz M, Okon T, Grady L, Harmison M, et al. Impact of COVID-19 on Cancer Care: How the Pandemic Is Delaying Cancer Diagnosis and Treatment for American Seniors. JCO Clin Cancer Inform. 2020;4:1059–71. [DOI] [PubMed] [PMC]
43. Luo Q, O'Connell DL, Yu XQ, Kahn C, Caruana M, Pesola F, et al. Cancer incidence and mortality in Australia from 2020 to 2044 and an exploratory analysis of the potential effect of treatment delays during the COVID-19 pandemic: a statistical modelling study. Lancet Public Health. 2022;7:e537–48. [DOI] [PubMed] [PMC]
44. Allahqoli L, Mazidimoradi A, Salehiniya H, Alkatout I. Impact of COVID-19 on cancer screening: a global perspective. Curr Opin Support Palliat Care. 2022;16:102–9. [DOI] [PubMed] [PMC]
45. Whittaker TM, Abdelrazek MEG, Fitzpatrick AJ, Froud JLJ, Kelly JR, Williamson JS, et al. Delay to elective colorectal cancer surgery and implications for survival: a systematic review and meta-analysis. Colorectal Dis. 2021;23:1699–711. [DOI] [PubMed] [PMC]
46. Fu R, Sutradhar R, Li Q, Hanna TP, Chan KKW, Irish JC, et al. Timeliness and Modality of Treatment for New Cancer Diagnoses During the COVID-19 Pandemic in Canada. JAMA Netw Open. 2023;6: e2250394. [DOI] [PubMed] [PMC]
47. Sathian B, Asim M, Banerjee I, Pizarro AB, Roy B, van Teijlingen ER, et al. Impact of COVID-19 on clinical trials and clinical research: A systematic review. Nepal J Epidemiol. 2020;10:878–87. [DOI] [PubMed] [PMC]
48. Daniels V, Saxena K, Roberts C, Kothari S, Corman S, Yao L, et al. Impact of reduced human papillomavirus vaccination coverage rates due to COVID-19 in the United States: A model based analysis. Vaccine. 2021;39:2731–5. [DOI] [PubMed] [PMC]
49. Pinato DJ, Scotti L, Gennari A, Colomba-Blameble E, Dolly S, Loizidou A, et al.; OnCovid study group. Determinants of enhanced vulnerability to coronavirus disease 2019 in UK patients with cancer: a European study. Eur J Cancer. 2021;150:190–202. [DOI] [PubMed] [PMC]
50. Castelo-Branco L, Tsourti Z, Gennatas S, Rogado J, Sekacheva M, Viñal D, et al. COVID-19 in patients with cancer: first report of the ESMO international, registry-based, cohort study (ESMO-CoCARE). ESMO Open. 2022;7:100499. [DOI] [PubMed] [PMC]
51. Khoury E, Nevitt S, Madsen WR, Turtle L, Davies G, Palmieri C. Differences in Outcomes and Factors Associated With Mortality Among Patients With SARS-CoV-2 Infection and Cancer Compared With Those Without Cancer: A Systematic Review and Meta-analysis. JAMA Netw Open. 2022;5:e2210880. [DOI] [PubMed] [PMC]
52. Klein IA, Rosenberg SM, Reynolds KL, Zubiri L, Rosovsky R, Piper-Vallillo AJ, et al. Impact of Cancer History on Outcomes Among Hospitalized Patients with COVID-19. Oncologist. 2021;26:685–93. [DOI] [PubMed] [PMC]
53. Sud A, Jones ME, Broggio J, Loveday C, Torr B, Garrett A, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. Ann Oncol. 2020;31:1065–74. [DOI] [PubMed] [PMC]
54. Bogaert B, Buisson V, Kozlakidis Z, Saintigny P. Organisation of cancer care in troubling times: A scoping review of expert guidelines and their implementation during the COVID-19 pandemic. Crit Rev Oncol Hematol. 2022;173:103656. [DOI] [PubMed] [PMC]
55. Boettcher AN, Hammoud DA, Weinberg JB, Agarwal P, Mendiratta-Lala M, Luker GD. Cancer Imaging and Patient Care during the COVID-19 Pandemic. Radiol Imaging Cancer. 2020;2:e200058. [DOI] [PubMed] [PMC]

56. Filip R, Gheorghita Puscaselu R, Anchidin-Norocel L, Dimian M, Savage WK. Global Challenges to Public Health Care Systems during the COVID-19 Pandemic: A Review of Pandemic Measures and Problems. J Pers Med. 2022;12:1295. [DOI] [PubMed] [PMC]
57. Keim-Malpass J, Vavolizza RD, Cohn WF, Kennedy EM, Showalter SL. Cancer Screening and Treatment Delays During the COVID-19 Pandemic and the Role of Health Literacy in Care Re-engagement: Findings from an NCI-Designated Comprehensive Cancer Center sample. J Cancer Educ. 2023;38:1405–12. [DOI] [PubMed] [PMC]
58. Mohseni Afshar Z, Hosseinzadeh R, Barary M, Ebrahimpour S, Alijanpour A, Sayad B, et al. Challenges posed by COVID-19 in cancer patients: A narrative review. Cancer Med. 2022;11:1119–35. [DOI] [PubMed] [PMC]
59. San Miguel Y, Gomez SL, Murphy JD, Schwab RB, McDaniels-Davidson C, Canchola AJ, et al. Age-related differences in breast cancer mortality according to race/ethnicity, insurance, and socioeconomic status. BMC Cancer. 2020;20:228. [DOI] [PubMed] [PMC]
60. Farshbafnadi M, Kamali Zonouzi S, Sabahi M, Dolatshahi M, Aarabi MH. Aging & COVID-19 susceptibility, disease severity, and clinical outcomes: The role of entangled risk factors. Exp Gerontol. 2021;154:111507. [DOI] [PubMed] [PMC]
61. Potter AL, Vaddaraju V, Venkateswaran S, Mansur A, Bajaj SS, Kiang MV, et al. Deaths Due to COVID-19 in Patients With Cancer During Different Waves of the Pandemic in the US. JAMA Oncol. 2023;9: 1417–22. [DOI] [PubMed] [PMC]
62. Bos MM, Verburg IW, Dumaij I, Stouthard J, Nortier JW, Richel D, et al. Intensive care admission of cancer patients: a comparative analysis. Cancer Med. 2015;4:966–76. [DOI] [PubMed] [PMC]
63. Plais H, Labruyere M, Creutin T, Nay P, Plantefeve G, Tapponnier R, et al. Outcomes of Patients With Active Cancer and COVID-19 in the Intensive-Care Unit: A Multicenter Ambispective Study. Front Oncol. 2022;12:858276. [DOI] [PubMed] [PMC]
64. Desai A, Gainor JF, Hegde A, Schram AM, Curigliano G, Pal S, et al.; COVID19 and Cancer Clinical Trials Working Group. COVID-19 vaccine guidance for patients with cancer participating in oncology clinical trials. Nat Rev Clin Oncol. 2021;18:313–9. [DOI] [PubMed] [PMC]
65. Wang L, Sun Y, Yuan Y, Mei Q, Yuan X. Clinical challenges in cancer patients with COVID-19: Aging, immunosuppression, and comorbidities. Aging (Albany NY). 2020;12:24462–74. [DOI] [PubMed] [PMC]
66. Sapna F, Deepa F, Sakshi F, Sonam F, Kiran F, Perkash RS, et al. Unveiling the Mysteries of Long COVID Syndrome: Exploring the Distinct Tissue and Organ Pathologies Linked to Prolonged COVID-19 Symptoms. Cureus. 2023;15:e44588. [DOI] [PubMed] [PMC]
67. Su Y, Yuan D, Chen DG, Ng RH, Wang K, Choi J, et al.; ISB-Swedish COVID-19 Biobanking Unit; Wrin T, Petropoulos CJ, Cole HR, Fischer TD, Wei W, Hoon DSB, et al. Multiple early factors anticipate post-acute COVID-19 sequelae. Cell. 2022;185:881–95.e20. [DOI] [PubMed] [PMC]
68. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27:601–15. [DOI] [PubMed] [PMC]
69. Wang C, Ramasamy A, Verduzco-Gutierrez M, Brode WM, Melamed E. Acute and post-acute sequelae of SARS-CoV-2 infection: a review of risk factors and social determinants. Virol J. 2023;20:124. [DOI] [PubMed] [PMC]
70. Huerne K, Filion KB, Grad R, Ernst P, Gershon AS, Eisenberg MJ. Epidemiological and clinical perspectives of long COVID syndrome. Am J Med Open. 2023;9:100033. [DOI] [PubMed] [PMC]
71. Mukherjee S, Pahan K. Is COVID-19 Gender-sensitive? J Neuroimmune Pharmacol. 2021;16:38–47. [DOI] [PubMed] [PMC]
72. Visweshwar N, Rico JF, Ayala I, Jaglal M, Laber DA, Ammad-Ud-Din M, et al. Insights into the Impact of Hesitancy on Cancer Care and COVID-19. Cancers (Basel). 2023;15:3115. [DOI] [PubMed] [PMC]

73. Thorat N, Pricl S, Parchur AK, Somvanshi SB, Li Q, Umrao S, et al. Safeguarding COVID-19 and cancer management: drug design and therapeutic approach. Open Res Eur. 2021;1:77. [DOI] [PubMed] [PMC]
74. Kim C, Moon JY, Kim SH, Kim SH, Chang Y, Cho WH, et al. Prevalences and Interrelationships of Post COVID-19 Fatigue, Sleep Disturbances, and Depression in Healthy Young and Middle-Aged Adults. J Clin Med. 2024;13:2801. [DOI] [PubMed] [PMC]
75. Menezes AS Jr, Botelho SM, Santos LR, Rezende AL. Acute COVID-19 Syndrome Predicts Severe Long COVID-19: An Observational Study. Cureus. 2022;14:e29826. [DOI] [PubMed] [PMC]
76. V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. Nat Rev Microbiol. 2021;19:155–70. [DOI] [PubMed] [PMC]
77. Jackson CB, Farzan M, Chen B, Choe H. Mechanisms of SARS-CoV-2 entry into cells. Nat Rev Mol Cell Biol. 2022;23:3–20. [DOI] [PubMed] [PMC]
78. Xia X. Domains and Functions of Spike Protein in Sars-Cov-2 in the Context of Vaccine Design. Viruses. 2021;13:109. [DOI] [PubMed] [PMC]
79. Mehrabadi ME, Hemmati R, Tashakor A, Homaei A, Yousefzadeh M, Hemati K, et al. Induced dysregulation of ACE2 by SARS-CoV-2 plays a key role in COVID-19 severity. Biomed Pharmacother. 2021;137:111363. [DOI] [PubMed] [PMC]
80. Triposkiadis F, Xanthopoulos A, Giamouzis G, Boudoulas KD, Starling RC, Skoularigis J, et al. ACE2, the Counter-Regulatory Renin-Angiotensin System Axis and COVID-19 Severity. J Clin Med. 2021;10:3885. [DOI] [PubMed] [PMC]
81. Gao X, Fang D, Liang Y, Deng X, Chen N, Zeng M, et al. Circular RNAs as emerging regulators in COVID-19 pathogenesis and progression. Front Immunol. 2022;13:980231. [DOI] [PubMed] [PMC]
82. Yang S, Zhou H, Liu M, Jaijyan D, Cruz-Cosme R, Ramasamy S, et al. SARS-CoV-2, SARS-CoV, and MERS-CoV encode circular RNAs of spliceosome-independent origin. J Med Virol. 2022;94:3203–22. [DOI] [PubMed] [PMC]
83. Zebardast A, Latifi T, Shirzad M, Goodarzi G, Ebrahimi Fana S, Samavarchi Tehrani S, et al. Critical involvement of circular RNAs in virus-associated cancers. Genes Dis. 2022;10:2296–305. [DOI] [PubMed] [PMC]
84. Rahmani-Kukia N, Abbasi A. New insights on circular RNAs and their potential applications as biomarkers, therapeutic agents, and preventive vaccines in viral infections: with a glance at SARS-CoV-2. Mol Ther Nucleic Acids. 2022;29:705–17. [DOI] [PubMed] [PMC]
85. Banu N, Panikar SS, Leal LR, Leal AR. Protective role of ACE2 and its downregulation in SARS-CoV-2 infection leading to Macrophage Activation Syndrome: Therapeutic implications. Life Sci. 2020;256:117905. [DOI] [PubMed] [PMC]
86. Wang CW, Chuang HC, Tan TH. ACE2 in chronic disease and COVID-19: gene regulation and post-translational modification. J Biomed Sci. 2023;30:71. [DOI] [PubMed] [PMC]
87. Hirano T. IL-6 in inflammation, autoimmunity and cancer. Int Immunol. 2021;33:127–48. [DOI] [PubMed] [PMC]
88. Jahankhani K, Ahangari F, Adcock IM, Mortaz E. Possible cancer-causing capacity of COVID-19: Is SARS-CoV-2 an oncogenic agent? Biochimie. 2023;213:130–8. [DOI] [PubMed] [PMC]
89. Rapti V, Tsaganos T, Vathiotis IA, Syrigos NK, Li P, Poulakou G. New Insights into SARS-CoV-2 and Cancer Cross-Talk: Does a Novel Oncogenesis Driver Emerge? Vaccines (Basel). 2022;10:1607. [DOI] [PubMed] [PMC]
90. Suryawanshi RK, Koganti R, Agelidis A, Patil CD, Shukla D. Dysregulation of Cell Signaling by SARS-CoV-2. Trends Microbiol. 2021;29:224–37. [DOI] [PubMed] [PMC]
91. Costanzo M, De Giglio MAR, Roviello GN. Deciphering the Relationship between SARS-CoV-2 and Cancer. Int J Mol Sci. 2023;24:7803. [DOI] [PubMed] [PMC]

92. ArulJothi KN, Kumaran K, Senthil S, Nidhu AB, Munaff N, Janitri VB, et al. Implications of reactive oxygen species in lung cancer and exploiting it for therapeutic interventions. Med Oncol. 2022;40:43. [DOI] [PubMed] [PMC]
93. Tutuncuoglu B, Cakir M, Batra J, Bouhaddou M, Eckhardt M, Gordon DE, et al. The Landscape of Human Cancer Proteins Targeted by SARS-CoV-2. Cancer Discov. 2020;10:916–21. [DOI] [PubMed] [PMC]
94. Walter M, Chen IP, Vallejo-Gracia A, Kim IJ, Bielska O, Lam VL, et al. SIRT5 is a proviral factor that interacts with SARS-CoV-2 Nsp14 protein. PLoS Pathog. 2022;18:e1010811. [DOI] [PubMed] [PMC]
95. Levine AJ, Berger SL. The interplay between epigenetic changes and the p53 protein in stem cells. Genes Dev. 2017;31:1195–201. [DOI] [PubMed] [PMC]
96. Maciejewski K, Giers M, Oleksiewicz U, Czerwinska P. The Epigenetic Modifiers HDAC2 and HDAC7 Inversely Associate with Cancer Stemness and Immunity in Solid Tumors. Int J Mol Sci. 2024;25:7841. [DOI] [PubMed] [PMC]
97. Hu B, Huang S, Yin L. The cytokine storm and COVID-19. J Med Virol. 2021;93:250–6. [DOI] [PubMed] [PMC]
98. Guo Q, Jin Y, Chen X, Ye X, Shen X, Lin M, et al. NF-κB in biology and targeted therapy: new insights and translational implications. Signal Transduct Target Ther. 2024;9:53. [DOI] [PubMed] [PMC]
99. Saini G, Aneja R. Cancer as a prospective sequela of long COVID-19. Bioessays. 2021;43:e2000331. [DOI] [PubMed] [PMC]
100. Ai Y, Wang H, Zheng Q, Li S, Liu J, Huang J, et al. Add fuel to the fire: Inflammation and immune response in lung cancer combined with COVID-19. Front Immunol. 2023;14:1174184. [DOI] [PubMed] [PMC]
101. Zhou Y, Liu Y, Gupta S, Paramo MI, Hou Y, Mao C, et al. A comprehensive SARS-CoV-2-human protein-protein interactome reveals COVID-19 pathobiology and potential host therapeutic targets. Nat Biotechnol. 2023;41:128–39. [DOI] [PubMed] [PMC]
102. Bhat S, Rishi P, Chadha VD. Understanding the epigenetic mechanisms in SARS CoV-2 infection and potential therapeutic approaches. Virus Res. 2022;318:198853. [DOI] [PubMed] [PMC]
103. Huang X, Liang H, Zhang H, Tian L, Cong P, Wu T, et al. The Potential Mechanism of Cancer Patients Appearing More Vulnerable to SARS-CoV-2 and Poor Outcomes: A Pan-Cancer Bioinformatics Analysis. Front Immunol. 2022;12:804387. [DOI] [PubMed] [PMC]
104. Sberna G, Maggi F, Amendola A. Virus-Encoded Circular RNAs: Role and Significance in Viral Infections. Int J Mol Sci. 2023;24:16547. [DOI] [PubMed] [PMC]
105. Stingi A, Cirillo L. SARS-CoV-2 infection and cancer: Evidence for and against a role of SARS-CoV-2 in cancer onset. Bioessays. 2021;43:e2000289. [DOI] [PubMed] [PMC]
106. Tsampasian V, Corballis N, Vassiliou VS. Renin-Angiotensin-Aldosterone Inhibitors and COVID-19 Infection. Curr Hypertens Rep. 2022;24:425–33. [DOI] [PubMed] [PMC]
107. Liu ZL, Chen HH, Zheng LL, Sun LP, Shi L. Angiogenic signaling pathways and anti-angiogenic therapy for cancer. Signal Transduct Target Ther. 2023;8:198. [DOI] [PubMed] [PMC]
108. Catarata MJ, Ribeiro R, Oliveira MJ, Robalo Cordeiro C, Medeiros R. Renin-Angiotensin System in Lung Tumor and Microenvironment Interactions. Cancers (Basel). 2020;12:1457. [DOI] [PubMed] [PMC]
109. Pallasch FB, Schumacher U. Angiotensin Inhibition, TGF-β and EMT in Cancer. Cancers (Basel). 2020;12:2785. [DOI] [PubMed] [PMC]
110. Laghlam D, Jozwiak M, Nguyen LS. Renin-Angiotensin-Aldosterone System and Immunomodulation: A State-of-the-Art Review. Cells. 2021;10:1767. [DOI] [PubMed] [PMC]
111. Madureira G, Soares R. The misunderstood link between SARS-CoV-2 and angiogenesis. A narrative review. Pulmonology. 2023;29:323–31. [DOI] [PubMed] [PMC]

112. Yu C, Tang W, Wang Y, Shen Q, Wang B, Cai C, et al. Downregulation of ACE2/Ang-(1-7)/Mas axis promotes breast cancer metastasis by enhancing store-operated calcium entry. Cancer Lett. 2016; 376:268–77. [DOI] [PubMed]
113. Al-Ewaidat OA, Gogia S, Begiashvili V, Naffaa MM. The multifaceted role of calcium signaling dynamics in neural cell proliferation and gliomagenesis. AIMS Biophysics. 2024;11:296–328. [DOI]
114. Wang X, Liu Y, Li K, Hao Z. Roles of p53-Mediated Host-Virus Interaction in Coronavirus Infection. Int J Mol Sci. 2023;24:6371. [DOI] [PubMed] [PMC]
115. Yoshimoto FK. The Proteins of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2 or n-COV19), the Cause of COVID-19. Protein J. 2020;39:198–216. [DOI] [PubMed] [PMC]
116. Cheng Y, He C, Wang M, Ma X, Mo F, Yang S, et al. Targeting epigenetic regulators for cancer therapy: mechanisms and advances in clinical trials. Signal Transduct Target Ther. 2019;4:62. [DOI] [PubMed] [PMC]
117. García-Carpizo V, Sarmentero J, Han B, Graña O, Ruiz-Llorente S, Pisano DG, et al. NSD2 contributes to oncogenic RAS-driven transcription in lung cancer cells through long-range epigenetic activation. Sci Rep. 2016;6:32952. [DOI] [PubMed] [PMC]
118. Balnis J, Madrid A, Hogan KJ, Drake LA, Chieng HC, Tiwari A, et al. Blood DNA methylation and COVID-19 outcomes. Clin Epigenetics. 2021;13:118. [DOI] [PubMed] [PMC]
119. Mazzoni A, Salvati L, Maggi L, Annunziato F, Cosmi L. Hallmarks of immune response in COVID-19: Exploring dysregulation and exhaustion. Semin Immunol. 2021;55:101508. [DOI] [PubMed] [PMC]
120. Ma J, Deng Y, Zhang M, Yu J. The role of multi-omics in the diagnosis of COVID-19 and the prediction of new therapeutic targets. Virulence. 2022;13:1101–10. [DOI] [PubMed] [PMC]
121. Harne R, Williams B, Abdelal HFM, Baldwin SL, Coler RN. SARS-CoV-2 infection and immune responses. AIMS Microbiol. 2023;9:245–76. [DOI] [PubMed] [PMC]
122. Li S, Du Z, Ma H, Cai L, Liu X, He J. Mendelian randomization provides causal association between COVID-19 and thyroid cancer: insights from a multi-cancer analysis. Front Oncol. 2024;14:1419020. [DOI] [PubMed] [PMC]
123. Wang D, Ma Y, Yan L, Gan W, Han Y, Tan JS, et al. Exploring the association between COVID-19 and male genital cancer risk in European population: evidence from mendelian randomization analysis. BMC Genom Data. 2023;24:56. [DOI] [PubMed] [PMC]
124. Cao H, Baranova A, Wei X, Wang C, Zhang F. Bidirectional causal associations between type 2 diabetes and COVID-19. J Med Virol. 2023;95:e28100. [DOI] [PubMed] [PMC]
125. Quan L, Tan J, Hua L, You X. Genetic predisposition between coronavirus disease 2019 and rheumatic diseases: A 2-sample Mendelian randomization study. Int J Rheum Dis. 2023;26:710–7. [DOI] [PubMed]
126. Li Z, Wei Y, Zhu G, Wang M, Zhang L. Cancers and COVID-19 Risk: A Mendelian Randomization Study. Cancers (Basel). 2022;14:2086. [DOI] [PubMed] [PMC]
127. Zhang Y, Mao Q, Li Y, Cheng J, Xia Q, Chen G, et al. Cancer and COVID-19 Susceptibility and Severity: A Two-Sample Mendelian Randomization and Bioinformatic Analysis. Front Cell Dev Biol. 2022;9: 759257. [DOI] [PubMed] [PMC]
128. Fanotto V, Ongaro E, Rihawi K, Avallone A, Silvestris N, Fornaro L, et al. HER-2 inhibition in gastric and colorectal cancers: tangible achievements, novel acquisitions and future perspectives. Oncotarget. 2016;7:69060–74. [DOI] [PubMed] [PMC]
129. Nagaraja V, Eslick GD. HER2 expression in gastric and oesophageal cancer: a meta-analytic review. J Gastrointest Oncol. 2015;6:143–54. [DOI] [PubMed] [PMC]
130. Michalski JE, Kurche JS, Schwartz DA. From ARDS to pulmonary fibrosis: the next phase of the COVID-19 pandemic? Transl Res. 2022;241:13–24. [DOI] [PubMed] [PMC]
131. Fattahi S, Khalifehzadeh-Esfahani Z, Mohammad-Rezaei M, Mafi S, Jafarinia M. PI3K/Akt/mTOR pathway: a potential target for anti-SARS-CoV-2 therapy. Immunol Res. 2022;70:269–75. [DOI] [PubMed] [PMC]

132. Deng X, Terunuma H, Nieda M. Exploring the Utility of NK Cells in COVID-19. Biomedicines. 2022;10:1002. [DOI] [PubMed] [PMC]
133. Vigerust DJ, Shepherd VL. Virus glycosylation: role in virulence and immune interactions. Trends Microbiol. 2007;15:211–8. [DOI] [PubMed] [PMC]
134. Zhou Q, Zhang L, Dong Y, Wang Y, Zhang B, Zhou S, et al. The role of SARS-CoV-2-mediated NF-κB activation in COVID-19 patients. Hypertens Res. 2024;47:375–84. [DOI] [PubMed] [PMC]
135. Fang C, Sun H, Wen J, Wu X, Wu Q, Zhai D. Investigation of the relationship between COVID-19 and pancreatic cancer using bioinformatics and systems biology approaches. Medicine (Baltimore). 2024;103:e39057. [DOI] [PubMed] [PMC]
136. Ebrahimi Sadrabadi A, Bereimipour A, Jalili A, Gholipurmalekabadi M, Farhadihosseinabadi B, Seifalian AM. The risk of pancreatic adenocarcinoma following SARS-CoV family infection. Sci Rep. 2021;11:12948. [DOI] [PubMed] [PMC]
137. Deng W, Bao L, Song Z, Zhang L, Yu P, Xu Y, et al. Infection with SARS-CoV-2 can cause pancreatic impairment. Signal Transduct Target Ther. 2024;9:98. [DOI] [PubMed] [PMC]
138. Howell MC, Green R, McGill AR, Dutta R, Mohapatra S, Mohapatra SS. SARS-CoV-2-Induced Gut Microbiome Dysbiosis: Implications for Colorectal Cancer. Cancers (Basel). 2021;13:2676. [DOI] [PubMed] [PMC]
139. Mozaffari SA, Salehi A, Mousavi E, Zaman BA, Nassaj AE, Ebrahimzadeh F, et al. SARS-CoV-2-associated gut microbiome alteration; A new contributor to colorectal cancer pathogenesis. Pathol Res Pract. 2022;239:154131. [DOI] [PubMed] [PMC]
140. Raj ST, Bruce AW, Anbalagan M, Srinivasan H, Chinnappan S, Rajagopal M, et al. COVID-19 influenced gut dysbiosis, post-acute sequelae, immune regulation, and therapeutic regimens. Front Cell Infect Microbiol. 2024;14:1384939. [DOI] [PubMed] [PMC]
141. Song Y, Huang T, Pan H, Du A, Wu T, Lan J, et al. The influence of COVID-19 on colorectal cancer was investigated using bioinformatics and systems biology techniques. Front Med (Lausanne). 2023;10:1169562. [DOI] [PubMed] [PMC]
142. Gopalakrishnan D, Sarode SC, Sarode GS, Sengupta N. COVID-19 and oral cancer: Critical viewpoint. World J Clin Oncol. 2022;13:725–8. [DOI] [PubMed] [PMC]
143. Nath S, Ferreira J, McVicar A, Oshilaja T, Swann B. Rise in oral cancer risk factors associated with the COVID-19 pandemic mandates a more diligent approach to oral cancer screening and treatment. J Am Dent Assoc. 2022;153:495–9. [DOI] [PubMed] [PMC]
144. Janczewski LM, Browner AE, Cotler JH, Palis BE, Chan K, Joung RH, et al. Survival Among Patients With High-Risk Gastrointestinal Cancers During the COVID-19 Pandemic. JAMA Netw Open. 2024;7:e240160. [DOI] [PubMed] [PMC]
145. Shigenobu Y, Miyamori D, Ikeda K, Yoshida S, Kikuchi Y, Kanno K, et al. Assessing the Influence of the COVID-19 Pandemic on Gastric Cancer Mortality Risk. J Clin Med. 2024;13:715. [DOI] [PubMed] [PMC]
146. Shafiee S, Cegolon L, Khafaei M, Gholami N, Zhao S, Khalesi N, et al. Gastrointestinal cancers, ACE-2/TMPRSS2 expression and susceptibility to COVID-19. Cancer Cell Int. 2021;21:431. [DOI] [PubMed] [PMC]
147. Troisi J, Venutolo G, Pujolassos Tanyà M, Delli Carri M, Landolfi A, Fasano A. COVID-19 and the gastrointestinal tract: Source of infection or merely a target of the inflammatory process following SARS-CoV-2 infection? World J Gastroenterol. 2021;27:1406–18. [DOI] [PubMed] [PMC]
148. Sacconi A, Donzelli S, Pulito C, Ferrero S, Spinella F, Morrone A, et al. TMPRSS2, a SARS-CoV-2 internalization protease is downregulated in head and neck cancer patients. J Exp Clin Cancer Res. 2020;39:200. [DOI] [PubMed] [PMC]
149. Liu X, Liu B, Shang Y, Cao P, Hou J, Chen F, et al. Decreased TMPRSS2 expression by SARS-CoV-2 predicts the poor prognosis of lung cancer patients through metabolic pathways and immune infiltration. Aging (Albany NY). 2022;14:73–108. [DOI] [PubMed] [PMC]

150. Day AT, Sher DJ, Lee RC, Truelson JM, Myers LL, Sumer BD, et al. Head and neck oncology during the COVID-19 pandemic: Reconsidering traditional treatment paradigms in light of new surgical and other multilevel risks. Oral Oncol. 2020;105:104684. [DOI] [PubMed] [PMC]
151. Samara P, Athanasopoulos M, Mastronikolis S, Kyrodimos E, Athanasopoulos I, Mastronikolis NS. The Role of Oncogenic Viruses in Head and Neck Cancers: Epidemiology, Pathogenesis, and Advancements in Detection Methods. Microorganisms. 2024;12:1482. [DOI] [PubMed] [PMC]
152. Sahu AK, Mathew R, Aggarwal P, Nayer J, Bhoi S, Satapathy S, et al. Clinical Determinants of Severe COVID-19 Disease - A Systematic Review and Meta-Analysis. J Glob Infect Dis. 2021;13:13–9. [DOI] [PubMed] [PMC]
153. Kocsmár É, Kocsmár I, Elamin F, Pápai L, Jakab Á, Várkonyi T, et al. Autopsy findings in cancer patients infected with SARS-CoV-2 show a milder presentation of COVID-19 compared to non-cancer patients. Geroscience. 2024;46:6101–14. [DOI] [PubMed] [PMC]
154. Kostoff RN, Briggs MB, Kanduc D, Shores DR, Kovatsi L, Drakoulis N, et al. Contributing factors common to COVID-19 and gastrointestinal cancer. Oncol Rep. 2022;47:16. [DOI] [PubMed] [PMC]
155. Velikova T, Snegarova V, Kukov A, Batselova H, Mihova A, Nakov R. Gastrointestinal mucosal immunity and COVID-19. World J Gastroenterol. 2021;27:5047–59. [DOI] [PubMed] [PMC]
156. Ogarek N, Oboza P, Olszanecka-Glinianowicz M, Kocelak P. SARS-CoV-2 infection as a potential risk factor for the development of cancer. Front Mol Biosci. 2023;10:1260776. [DOI] [PubMed] [PMC]
157. Khiali S, Rezagholizadeh A, Entezari-Maleki T. SARS-CoV-2 and probable lung cancer risk. Bioimpacts. 2022;12:291–2. [DOI] [PubMed] [PMC]
158. Sadhukhan P, Ugurlu MT, Hoque MO. Effect of COVID-19 on Lungs: Focusing on Prospective Malignant Phenotypes. Cancers (Basel). 2020;12:3822. [DOI] [PubMed] [PMC]
159. Thapa R, Gupta S, Gupta G, Bhat AA, Smriti, Singla M, et al. Epithelial-mesenchymal transition to mitigate age-related progression in lung cancer. Ageing Res Rev. 2024;102:102576. [DOI] [PubMed]
160. Liapis I, Baritaki S. COVID-19 vs. Cancer Immunosurveillance: A Game of Thrones within an Inflamed Microenviroment. Cancers (Basel). 2022;14:4330. [DOI] [PubMed] [PMC]
161. Yu W, Tu Y, Long Z, Liu J, Kong D, Peng J, et al. Reactive Oxygen Species Bridge the Gap between Chronic Inflammation and Tumor Development. Oxid Med Cell Longev. 2022;2022:2606928. [DOI] [PubMed] [PMC]
162. Ahmed SA, Alahmadi YM, Abdou YA. The Impact of Serum Levels of Reactive Oxygen and Nitrogen Species on the Disease Severity of COVID-19. Int J Mol Sci. 2023;24:8973. [DOI] [PubMed] [PMC]
163. Huang HC, Liao CC, Wang SH, Lee IJ, Lee TA, Hsu JM, et al. Hyperglycosylated spike of SARS-CoV-2 gamma variant induces breast cancer metastasis. Am J Cancer Res. 2021;11:4994–5005. [PubMed] [PMC]
164. Balamurugan K, Poria DK, Sehareen SW, Krishnamurthy S, Tang W, McKennett L, et al. Stabilization of E-cadherin adhesions by COX-2/GSK3β signaling is a targetable pathway in metastatic breast cancer. JCI Insight. 2023;8:e156057. [DOI] [PubMed] [PMC]
165. Jiang Y, Chen L, Shen J, Mei X, Yao J, Chen T, et al. The potential role of abnormal angiotensin-converting enzyme 2 expression correlated with immune infiltration after SARS-CoV-2 infection in the prognosis of breast cancer. Aging (Albany NY). 2021;13:20886–95. [DOI] [PubMed] [PMC]
166. Wu CT, Lidsky PV, Xiao Y, Lee IT, Cheng R, Nakayama T, et al. SARS-CoV-2 infects human pancreatic β cells and elicits β cell impairment. Cell Metab. 2021;33:1565–76.e5. [DOI] [PubMed] [PMC]
167. Niekamp P, Kim CH. Microbial Metabolite Dysbiosis and Colorectal Cancer. Gut Liver. 2023;17:190–203. [DOI] [PubMed] [PMC]
168. Villapol S. Gastrointestinal symptoms associated with COVID-19: impact on the gut microbiome. Transl Res. 2020;226:57–69. [DOI] [PubMed] [PMC]
169. Martelli-Júnior H, Machado RA, Martelli DRB, Andrade MC, Coletta RD. Oral cancer and ACE2 receptor of SARS-CoV-2. Oral Oncol. 2020;108:104920. [DOI] [PubMed] [PMC]

170. Giobbe GG, Bonfante F, Jones BC, Gagliano O, Luni C, Zambaiti E, et al. SARS-CoV-2 infection and replication in human gastric organoids. Nat Commun. 2021;12:6610. [DOI] [PubMed] [PMC]
171. Javier RT, Butel JS. The history of tumor virology. Cancer Res. 2008;68:7693–706. [DOI] [PubMed] [PMC]
172. Schiller JT, Lowy DR. An Introduction to Virus Infections and Human Cancer. Recent Results Cancer Res. 2021;217:1–11. [DOI] [PubMed] [PMC]
173. Chigbu DI, Loonawat R, Sehgal M, Patel D, Jain P. Hepatitis C Virus Infection: Host–Virus Interaction and Mechanisms of Viral Persistence. Cells. 2019;8:376. [DOI] [PubMed] [PMC]
174. Peluso MJ, Ryder D, Flavell RR, Wang Y, Levi J, LaFranchi BH, et al. Tissue-based T cell activation and viral RNA persist for up to 2 years after SARS-CoV-2 infection. Sci Transl Med. 2024;16:eadk3295. [DOI] [PubMed] [PMC]
175. Wu W, Cheng Y, Zhou H, Sun C, Zhang S. The SARS-CoV-2 nucleocapsid protein: its role in the viral life cycle, structure and functions, and use as a potential target in the development of vaccines and diagnostics. Virol J. 2023;20:6. [DOI] [PubMed] [PMC]
176. Greten FR, Grivennikov SI. Inflammation and Cancer: Triggers, Mechanisms, and Consequences. Immunity. 2019;51:27–41. [DOI] [PubMed] [PMC]
177. Zhao H, Wu L, Yan G, Chen Y, Zhou M, Wu Y, et al. Inflammation and tumor progression: signaling pathways and targeted intervention. Signal Transduct Target Ther. 2021;6:263. [DOI] [PubMed] [PMC]
178. du Plessis M, Fourie C, Riedemann J, de Villiers WJS, Engelbrecht AM. Cancer and Covid-19: Collectively catastrophic. Cytokine Growth Factor Rev. 2022;63:78–89. [DOI] [PubMed] [PMC]
179. Yunis J, Short KR, Yu D. Severe respiratory viral infections: T-cell functions diverging from immunity to inflammation. Trends Microbiol. 2023;31:644–56. [DOI] [PubMed] [PMC]
180. Gonzalez H, Hagerling C, Werb Z. Roles of the immune system in cancer: from tumor initiation to metastatic progression. Genes Dev. 2018;32:1267–84. [DOI] [PubMed] [PMC]
181. Sorrenti V, Buriani A, Fortinguerra S, Davinelli S, Scapagnini G, Cassidy A, et al. Cell Survival, Death, and Proliferation in Senescent and Cancer Cells: the Role of (Poly)phenols. Adv Nutr. 2023;14:1111–30. [DOI] [PubMed] [PMC]
182. Wang B, Han J, Elisseeff JH, Demaria M. The senescence-associated secretory phenotype and its physiological and pathological implications. Nat Rev Mol Cell Biol. 2024;25:958–78. [DOI] [PubMed]
183. Milanovic M, Fan DNY, Belenki D, Däbritz JHM, Zhao Z, Yu Y, et al. Senescence-associated reprogramming promotes cancer stemness. Nature. 2018;553:96–100. [DOI] [PubMed]
184. Ye R, Wang A, Bu B, Luo P, Deng W, Zhang X, et al. Viral oncogenes, viruses, and cancer: a third-generation sequencing perspective on viral integration into the human genome. Front Oncol. 2023;13:1333812. [DOI] [PubMed] [PMC]
185. Dong W, Wang H, Li M, Li P, Ji S. Virus-induced host genomic remodeling dysregulates gene expression, triggering tumorigenesis. Front Cell Infect Microbiol. 2024;14:1359766. [DOI] [PubMed] [PMC]
186. Ahmad L, Mostowy S, Sancho-Shimizu V. Autophagy-Virus Interplay: From Cell Biology to Human Disease. Front Cell Dev Biol. 2018;6:155. [DOI] [PubMed] [PMC]
187. Vitto VAM, Bianchin S, Zolondick AA, Pellielo G, Rimessi A, Chianese D, et al. Molecular Mechanisms of Autophagy in Cancer Development, Progression, and Therapy. Biomedicines. 2022;10:1596. [DOI] [PubMed] [PMC]
188. Bhutia SK, Mukhopadhyay S, Sinha N, Das DN, Panda PK, Patra SK, et al. Autophagy: cancer's friend or foe? Adv Cancer Res. 2013;118:61–95. [DOI] [PubMed] [PMC]
189. Krump NA, You J. Molecular mechanisms of viral oncogenesis in humans. Nat Rev Microbiol. 2018;16:684–98. [DOI] [PubMed] [PMC]
190. Davis HE, McCorkell L, Vogel JM, Topol EJ. Author Correction: Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023;21:408. [DOI] [PubMed] [PMC]

191. Wang L, Xiang Y. Spike Glycoprotein-Mediated Entry of SARS Coronaviruses. Viruses. 2020;12:1289. [DOI] [PubMed] [PMC]
192. Antony P, Vijayan R. Role of SARS-CoV-2 and ACE2 variations in COVID-19. Biomed J. 2021;44: 235–44. [DOI] [PubMed] [PMC]
193. Suvarnapathaki S, Chauhan D, Nguyen A, Ramalingam M, Camci-Unal G. Advances in Targeting ACE2 for Developing COVID-19 Therapeutics. Ann Biomed Eng. 2022;50:1734–49. [DOI] [PubMed] [PMC]
194. Lynch SM, Guo G, Gibson DS, Bjourson AJ, Rai TS. Role of Senescence and Aging in SARS-CoV-2 Infection and COVID-19 Disease. Cells. 2021;10:3367. [DOI] [PubMed] [PMC]
195. Mohiuddin M, Kasahara K. The emerging role of cellular senescence in complications of COVID-19. Cancer Treat Res Commun. 2021;28:100399. [DOI] [PubMed] [PMC]
196. Kumari R, Jat P. Mechanisms of Cellular Senescence: Cell Cycle Arrest and Senescence Associated Secretory Phenotype. Front Cell Dev Biol. 2021;9:645593. [DOI] [PubMed] [PMC]
197. Coppé JP, Desprez PY, Krtolica A, Campisi J. The senescence-associated secretory phenotype: the dark side of tumor suppression. Annu Rev Pathol. 2010;5:99–118. [DOI] [PubMed] [PMC]
198. Dong Z, Luo Y, Yuan Z, Tian Y, Jin T, Xu F. Cellular senescence and SASP in tumor progression and therapeutic opportunities. Mol Cancer. 2024;23:181. [DOI] [PubMed] [PMC]
199. Li X, Li C, Zhang W, Wang Y, Qian P, Huang H. Inflammation and aging: signaling pathways and intervention therapies. Signal Transduct Target Ther. 2023;8:239. [DOI] [PubMed] [PMC]
200. Hibino S, Kawazoe T, Kasahara H, Itoh S, Ishimoto T, Sakata-Yanagimoto M, et al. Inflammation-Induced Tumorigenesis and Metastasis. Int J Mol Sci. 2021;22:5421. [DOI] [PubMed] [PMC]
201. Dettorre GM, Dolly S, Loizidou A, Chester J, Jackson A, Mukherjee U, et al.; OnCovid study group. Systemic pro-inflammatory response identifies patients with cancer with adverse outcomes from SARS-CoV-2 infection: the OnCovid Inflammatory Score. J Immunother Cancer. 2021;9:e002277. [DOI] [PubMed] [PMC]
202. Tandon P, Abrams ND, Avula LR, Carrick DM, Chander P, Divi RL, et al. Unraveling Links between Chronic Inflammation and Long COVID: Workshop Report. J Immunol. 2024;212:505–12. [DOI] [PubMed]
203. Sohrab SS, Raj R, Nagar A, Hawthorne S, Paiva-Santos AC, Kamal MA, et al. Chronic Inflammation's Transformation to Cancer: A Nanotherapeutic Paradigm. Molecules. 2023;28:4413. [DOI] [PubMed] [PMC]
204. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell. 2010;140:883–99. [DOI] [PubMed] [PMC]
205. Lemon SM, McGivern DR. Is hepatitis C virus carcinogenic? Gastroenterology. 2012;142:1274–8. [DOI] [PubMed] [PMC]
206. Cheung CCL, Goh D, Lim X, Tien TZ, Lim JCT, Lee JN, et al. Residual SARS-CoV-2 viral antigens detected in GI and hepatic tissues from five recovered patients with COVID-19. Gut. 2022;71:226–9. [DOI] [PubMed]
207. Ploss A, Kapoor A. Animal Models of Hepatitis C Virus Infection. Cold Spring Harb Perspect Med. 2020;10:a036970. [DOI] [PubMed] [PMC]
208. Pandya PH, Murray ME, Pollok KE, Renbarger JL. The Immune System in Cancer Pathogenesis: Potential Therapeutic Approaches. J Immunol Res. 2016;2016:4273943. [DOI] [PubMed] [PMC]
209. Pardoll D. Cancer and the Immune System: Basic Concepts and Targets for Intervention. Semin Oncol. 2015;42:523–38. [DOI] [PubMed] [PMC]
210. Jalloh S, Olejnik J, Berrigan J, Nisa A, Suder EL, Akiyama H, et al. CD169-mediated restrictive SARS-CoV-2 infection of macrophages induces pro-inflammatory responses. PLoS Pathog. 2022;18: e1010479. [DOI] [PubMed] [PMC]
211. Ricci D, Etna MP, Rizzo F, Sandini S, Severa M, Coccia EM. Innate Immune Response to SARS-CoV-2 Infection: From Cells to Soluble Mediators. Int J Mol Sci. 2021;22:7017. [DOI] [PubMed] [PMC]

212. Knoll R, Schultze JL, Schulte-Schrepping J. Monocytes and Macrophages in COVID-19. Front Immunol. 2021;12:720109. [DOI] [PubMed] [PMC]
213. Opsteen S, Files JK, Fram T, Erdmann N. The role of immune activation and antigen persistence in acute and long COVID. J Investig Med. 2023;71:545–62. [DOI] [PubMed] [PMC]
214. Behura A, Naik L, Patel S, Das M, Kumar A, Mishra A, et al. Involvement of epigenetics in affecting host immunity during SARS-CoV-2 infection. Biochim Biophys Acta Mol Basis Dis. 2023;1869: 166634. [DOI] [PubMed] [PMC]
215. Sayahinouri M, Mashayekhi Firouz S, Ebrahimi Sadrabadi A, Masoudnia M, Abdolahi M, Jafarzadeh F, et al. Functionality of immune cells in COVID-19 infection: development of cell-based therapeutics. Bioimpacts. 2023;13:159–79. [DOI] [PubMed] [PMC]
216. Klein J, Wood J, Jaycox JR, Dhodapkar RM, Lu P, Gehlhausen JR, et al. Distinguishing features of long COVID identified through immune profiling. Nature. 2023;623:139–48. [DOI] [PubMed] [PMC]
217. Ivanova T, Mariienko Y, Mehterov N, Kazakova M, Sbirkov Y, Todorova K, et al. Autophagy and SARS-CoV-2-Old Players in New Games. Int J Mol Sci. 2023;24:7734. [DOI] [PubMed] [PMC]
218. Resnik R, Lopez Mingorance F, Rivera F, Mitchell F, Gonzalez CD, Vaccaro MI. Autophagy in Inflammatory Response against SARS-CoV-2. Int J Mol Sci. 2023;24:4928. [DOI] [PubMed] [PMC]
219. Habibzadeh P, Dastsooz H, Eshraghi M, Łos MJ, Klionsky DJ, Ghavami S. Autophagy: The Potential Link between SARS-CoV-2 and Cancer. Cancers (Basel). 2021;13:5721. [DOI] [PubMed] [PMC]
220. Moriyama M, Lucas C, Monteiro VS; Yale SARS-CoV-2 Genomic Surveillance Initiative; Iwasaki A. Enhanced inhibition of MHC-I expression by SARS-CoV-2 Omicron subvariants. Proc Natl Acad Sci U S A. 2023;120:e2221652120. [DOI] [PubMed] [PMC]
221. Paunovic V, Vucicevic L, Misirkic Marjanovic M, Perovic V, Ristic B, et al. Autophagy Receptor p62 Regulates SARS-CoV-2-Induced Inflammation in COVID-19. Cells. 2023;12:1282. [DOI] [PubMed] [PMC]
222. Puissant A, Fenouille N, Auberger P. When autophagy meets cancer through p62/SQSTM1. Am J Cancer Res. 2012;2:397–413. [PubMed] [PMC]
223. Fillmore NR, La J, Szalat RE, Tuck DP, Nguyen V, Yildirim C, et al. Prevalence and Outcome of COVID-19 Infection in Cancer Patients: A National Veterans Affairs Study. J Natl Cancer Inst. 2021;113: 691–8. [DOI] [PubMed] [PMC]
224. Liu B, Zhou H, Tan L, Siu KTH, Guan XY. Exploring treatment options in cancer: Tumor treatment strategies. Signal Transduct Target Ther. 2024;9:175. [DOI] [PubMed] [PMC]
225. Andraska EA, Alabi O, Dorsey C, Erben Y, Velazquez G, Franco-Mesa C, et al. Health care disparities during the COVID-19 pandemic. Semin Vasc Surg. 2021;34:82–8. [DOI] [PubMed] [PMC]
226. Aleshina OA, Zakurdaeva K, Vasileva AN, Dubov SK, Dubov VS, Vorobyev VI, et al. Clinical Outcomes in Patients With COVID-19 and Hematologic Disease. Clin Lymphoma Myeloma Leuk. 2023;23: 589–98. [DOI] [PubMed] [PMC]
227. Pagano L, Salmanton-García J, Marchesi F, Busca A, Corradini P, Hoenigl M, et al.; EPICOVIDEHA working group. COVID-19 infection in adult patients with hematological malignancies: a European Hematology Association Survey (EPICOVIDEHA). J Hematol Oncol. 2021;14:168. [DOI] [PubMed] [PMC]
228. Martínez-López J, De la Cruz J, Gil-Manso R, Alegre A, Ortiz J, Llamas P, et al.; Asociación Madrileña de Hematología y Hemoterapia (AMHH). COVID-19 Severity and Survival over Time in Patients with Hematologic Malignancies: A Population-Based Registry Study. Cancers (Basel). 2023;15:1497. [DOI] [PubMed] [PMC]
229. Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, et al. Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study during the COVID-19 Outbreak. Cancer Discov. 2020;10:783–91. [DOI] [PubMed] [PMC]

230. Passaro A, Bestvina C, Velez Velez M, Garassino MC, Garon E, Peters S. Severity of COVID-19 in patients with lung cancer: evidence and challenges. J Immunother Cancer. 2021;9:e002266. [DOI] [PubMed] [PMC]
231. Whisenant JG, Trama A, Torri V, De Toma A, Viscardi G, Cortellini A, et al. TERAVOLT: Thoracic Cancers International COVID-19 Collaboration. Cancer Cell. 2020;37:742–5. [DOI] [PubMed] [PMC]
232. Jee J, Foote MB, Lumish M, Stonestrom AJ, Wills B, Narendra V, et al. Chemotherapy and COVID-19 Outcomes in Patients With Cancer. J Clin Oncol. 2020;38:3538–46. [DOI] [PubMed] [PMC]
233. Gulati S, Muddasani R, Gustavo Bergerot P, Pal SK. Systemic therapy and COVID19: Immunotherapy and chemotherapy. Urol Oncol. 2021;39:213–20. [DOI] [PubMed] [PMC]
234. Wu Q, Luo S, Xie X. The impact of anti-tumor approaches on the outcomes of cancer patients with COVID-19: a meta-analysis based on 52 cohorts incorporating 9231 participants. BMC Cancer. 2022; 22:241. [DOI] [PubMed] [PMC]
235. Curigliano G, Banerjee S, Cervantes A, Garassino MC, Garrido P, Girard N, et al.; Panel members. Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. Ann Oncol. 2020;31:1320–35. [DOI] [PubMed] [PMC]
236. Lee LY, Cazier JB, Angelis V, Arnold R, Bisht V, Campton NA, et al.; UK Coronavirus Monitoring Project Team; Kerr R, Middleton G. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet. 2020;395:1919–26. [DOI] [PubMed] [PMC]
237. Lee LYW, Cazier JB, Starkey T, Briggs SEW, Arnold R, Bisht V, et al.; UK Coronavirus Cancer Monitoring Project Team. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. Lancet Oncol. 2020;21:1309–16. [DOI] [PubMed] [PMC]
238. Lisco G, De Tullio A, Stragapede A, Solimando AG, Albanese F, Capobianco M, et al. COVID-19 and the Endocrine System: A Comprehensive Review on the Theme. J Clin Med. 2021;10:2920. [DOI] [PubMed] [PMC]
239. Puig-Domingo M, Marazuela M, Yildiz BO, Giustina A. COVID-19 and endocrine and metabolic diseases. An updated statement from the European Society of Endocrinology. Endocrine. 2021;72: 301–16. [DOI] [PubMed] [PMC]
240. Boughey JC, Snyder RA, Kantor O, Zheng L, Chawla A, Nguyen TT, et al. Impact of the COVID-19 Pandemic on Cancer Clinical Trials. Ann Surg Oncol. 2021;28:7311–6. [DOI] [PubMed] [PMC]
241. Abdelkader H, El-Kassas M. Tailored treatment strategies for cancer patients during COVID-19 pandemic. Rep Pract Oncol Radiother. 2022;27:318–30. [DOI] [PubMed] [PMC]
242. Jafari-Gharabaghlou D, Dadashpour M, Khanghah OJ, Salmani-Javan E, Zarghami N. Potentiation of Folate-Functionalized PLGA-PEG nanoparticles loaded with metformin for the treatment of breast Cancer: possible clinical application. Mol Biol Rep. 2023;50:3023–33. [DOI] [PubMed]
243. Khoshravan L, Dadashpour M, Hashemi M, Zarghami N. Design and Development of Nanostructured Co Delivery of Artemisinin and Chrysin for Targeting hTERT Gene Expression in Breast Cancer Cell Line: Possible Clinical Application in Cancer Treatment. Asian Pac J Cancer Prev. 2022;23:919–27. [DOI] [PubMed] [PMC]
244. Cen X, Wang F, Huang X, Jovic D, Dubee F, Yang H, et al. Towards precision medicine: Omics approach for COVID-19. Biosaf Health. 2023;5:78–88. [DOI] [PubMed] [PMC]
245. Thomas S, Sagan A, Larkin J, Cylus J, Figueras J, Karanikolos M. Strengthening health systems resilience: Key concepts and strategies. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2020. [PubMed]
246. Garfan S, Alamoodi AH, Zaidan BB, Al-Zobbi M, Hamid RA, Alwan JK, et al. Telehealth utilization during the Covid-19 pandemic: A systematic review. Comput Biol Med. 2021;138:104878. [DOI] [PubMed] [PMC]

247. Toni E, Ayatollahi H. An insight into the use of telemedicine technology for cancer patients during the Covid-19 pandemic: a scoping review. BMC Med Inform Decis Mak. 2024;24:104. [DOI] [PubMed] [PMC]
248. Baron R, Haick H. Mobile Diagnostic Clinics. ACS Sens. 2024;9:2777–92. [DOI] [PubMed] [PMC]
249. Parikh RB, Basen-Enquist KM, Bradley C, Estrin D, Levy M, Lichtenfeld JL, et al. Digital Health Applications in Oncology: An Opportunity to Seize. J Natl Cancer Inst. 2022;114:1338–9. [DOI] [PubMed] [PMC]
250. Petrova E, Farinholt T, Joshi TP, Moreno H, Al Mohajer M, Patel SM, et al. A Community-Based Management of COVID-19 in a Mobile Container Unit. Vaccines (Basel). 2021;9:1362. [DOI] [PubMed] [PMC]
251. Al Harbi S, Aljohani B, Elmasry L, Baldovino FL, Raviz KB, Altowairqi L, et al. Streamlining patient flow and enhancing operational efficiency through case management implementation. BMJ Open Qual. 2024;13:e002484. [DOI] [PubMed] [PMC]
252. Lustberg MB, Kuderer NM, Desai A, Bergerot C, Lyman GH. Mitigating long-term and delayed adverse events associated with cancer treatment: implications for survivorship. Nat Rev Clin Oncol. 2023;20:527–42. [DOI] [PubMed] [PMC]
253. Toh ZQ, Russell FM, Garland SM, Mulholland EK, Patton G, Licciardi PV. Human Papillomavirus Vaccination After COVID-19. JNCI Cancer Spectr. 2021;5:pkab011. [DOI] [PubMed] [PMC]
254. Smulian EA, Mitchell KR, Stokley S. Interventions to increase HPV vaccination coverage: A systematic review. Hum Vaccin Immunother. 2016;12:1566–88. [DOI] [PubMed] [PMC]
255. Basu S, Ashok G, Debroy R, Ramaiah S, Livingstone P, Anbarasu A. Impact of the COVID-19 pandemic on routine vaccine landscape: A global perspective. Hum Vaccin Immunother. 2023;19:2199656. [DOI] [PubMed] [PMC]
256. Fasano GA, Bayard S, Bea VJ. Breast Cancer Disparities and the COVID-19 Pandemic. Curr Breast Cancer Rep. 2022;14:192–8. [DOI] [PubMed] [PMC]
257. Patel MI, Lopez AM, Blackstock W, Reeder-Hayes K, Moushey EA, Phillips J, et al. Cancer Disparities and Health Equity: A Policy Statement From the American Society of Clinical Oncology. J Clin Oncol. 2020;38:3439–48. [DOI] [PubMed] [PMC]
258. Kale S, Hirani S, Vardhan S, Mishra A, Ghode DB, Prasad R, et al. Addressing Cancer Disparities Through Community Engagement: Lessons and Best Practices. Cureus. 2023;15:e43445. [DOI] [PubMed] [PMC]
259. Rucinska M, Nawrocki S. COVID-19 Pandemic: Impact on Cancer Patients. Int J Environ Res Public Health. 2022;19:12470. [DOI] [PubMed] [PMC]
260. Peluso MJ, Deeks SG. Mechanisms of long COVID and the path toward therapeutics. Cell. 2024;187:5500–29. [DOI] [PubMed] [PMC]
261. Chamilos G, Lionakis MS, Kontoyiannis DP. Are All Patients with Cancer at Heightened Risk for Severe Coronavirus Disease 2019 (COVID-19)? Clin Infect Dis. 2021;72:351–6. [DOI] [PubMed] [PMC]
262. Ippolito E, Fiore M, Greco C, D'Angelillo RM, Ramella S. COVID-19 and radiation induced pneumonitis: Overlapping clinical features of different diseases. Radiother Oncol. 2020;148:201–2. [DOI] [PubMed] [PMC]
263. Pezeshki PS, Rezaei N. Immune checkpoint inhibition in COVID-19: risks and benefits. Expert Opin Biol Ther. 2021;21:1173–9. [DOI] [PubMed] [PMC]
264. Wagner C, Griesel M, Mikolajewska A, Metzendorf MI, Fischer AL, Stegemann M, et al. Systemic corticosteroids for the treatment of COVID-19: Equity-related analyses and update on evidence. Cochrane Database Syst Rev. 2022;11:CD014963. [DOI] [PubMed] [PMC]
265. Marušić J, Hasković E, Mujezinović A, Đido V. Correlation of pre-existing comorbidities with disease severity in individuals infected with SARS-COV-2 virus. BMC Public Health. 2024;24:1053. [DOI] [PubMed] [PMC]

266. Tsampasian V, Elghazaly H, Chattopadhyay R, Debski M, Naing TKP, Garg P, et al. Risk Factors Associated With Post-COVID-19 Condition: A Systematic Review and Meta-analysis. JAMA Intern Med. 2023;183:566–80. [DOI] [PubMed] [PMC]
267. De Winter FHR, Hotterbeekx A, Huizing MT, Konnova A, Fransen E, Jongers B, et al. Blood Cytokine Analysis Suggests That SARS-CoV-2 Infection Results in a Sustained Tumour Promoting Environment in Cancer Patients. Cancers (Basel). 2021;13:5718. [DOI] [PubMed] [PMC]
268. Canale MP, Menghini R, Martelli E, Federici M. COVID-19-Associated Endothelial Dysfunction and Microvascular Injury: From Pathophysiology to Clinical Manifestations. Card Electrophysiol Clin. 2022;14:21–8. [DOI] [PubMed] [PMC]
269. Nunn AVW, Guy GW, Brysch W, Bell JD. Understanding Long COVID; Mitochondrial Health and Adaptation-Old Pathways, New Problems. Biomedicines. 2022;10:3113. [DOI] [PubMed] [PMC]
270. Ciarambino T, Para O, Giordano M. Immune system and COVID-19 by sex differences and age. Womens Health (Lond). 2021;17:17455065211022262. [DOI] [PubMed] [PMC]
271. Attieh S, Loiselle CG. Cancer Care Team Functioning during COVID-19: A Narrative Literature Review and Synthesis. Curr Oncol. 2024;31:335–49. [DOI] [PubMed] [PMC]
272. Croswell JM, Corley DA, Lafata JE, Haas JS, Inadomi JM, Kamineni A, et al.; National Cancer Institute Population-based Research to Optimize the Screening Process (PROSPR) II Consortium. Cancer screening in the U.S. through the COVID-19 pandemic, recovery, and beyond. Prev Med. 2021;151: 106595. [DOI] [PubMed] [PMC]
273. Yeoh K, Wu Y, Chakraborty S, Elhusseiny G, Gondhowiardjo S, Joseph N, et al. Global Health System Resilience during Encounters with Stressors - Lessons Learnt from Cancer Services during the COVID-19 Pandemic. Clin Oncol (R Coll Radiol). 2023;35:e289–300. [DOI] [PubMed] [PMC]
274. Shaffer KM, Turner KL, Siwik C, Gonzalez BD, Upasani R, Glazer JV, et al. Digital health and telehealth in cancer care: a scoping review of reviews. Lancet Digit Health. 2023;5:e316–27. [DOI] [PubMed] [PMC]
275. Eisman AB, Kim B, Salloum RG, Shuman CJ, Glasgow RE. Advancing rapid adaptation for urgent public health crises: Using implementation science to facilitate effective and efficient responses. Front Public Health. 2022;10:959567. [DOI] [PubMed] [PMC]
276. Doshi SD, Bange EM, Daly B, Kuperman G, Panageas KS, Morris MJ. Telemedicine and Cancer Care: Barriers and Strategies to Optimize Delivery. Cancer J. 2024;30:8–15. [DOI] [PubMed] [PMC]
277. Jazieh AR, Akbulut H, Curigliano G, Rogado A, Alsharm AA, Razis ED, et al.; International Research Network on COVID-19 Impact on Cancer Care. Impact of the COVID-19 Pandemic on Cancer Care: A Global Collaborative Study. JCO Glob Oncol. 2020;6:1428–38. [DOI] [PubMed] [PMC]
278. Druedahl LC, Minssen T, Price WN. Collaboration in times of crisis: A study on COVID-19 vaccine R& D partnerships. Vaccine. 2021;39:6291–5. [DOI] [PubMed] [PMC]
279. Nana-Sinkam P, Kraschnewski J, Sacco R, Chavez J, Fouad M, Gal T, et al. Health disparities and equity in the era of COVID-19. J Clin Transl Sci. 2021;5:e99. [DOI] [PubMed] [PMC]
280. Mohamadi E, Olyaeemanesh A, Takian A, Yaftian F, Kiani MM, Larijani B. Short and Long-term Impacts of COVID-19 Pandemic on Health Equity: A Comprehensive Review. Med J Islam Repub Iran. 2022;36:179. [DOI] [PubMed] [PMC]
281. Bakouny Z, Hawley JE, Choueiri TK, Peters S, Rini BI, Warner JL, et al. COVID-19 and Cancer: Current Challenges and Perspectives. Cancer Cell. 2020;38:629–46. [DOI] [PubMed] [PMC]
282. Broom A, Williams Veazey L, Kenny K, Harper I, Peterie M, Page A, et al. The Enduring Effects of COVID for Cancer Care: Learning from Real-Life Clinical Practice. Clin Cancer Res. 2023;29:1670–7. [DOI] [PubMed] [PMC]
283. Liu D, Che X, Wang X, Ma C, Wu G. Tumor Vaccines: Unleashing the Power of the Immune System to Fight Cancer. Pharmaceuticals (Basel). 2023;16:1384. [DOI] [PubMed] [PMC]
284. Kamboj M, Bohlke K, Baptiste DM, Dunleavy K, Fueger A, Jones L, et al. Vaccination of Adults With Cancer: ASCO Guideline. J Clin Oncol. 2024;42:1699–721. [DOI] [PubMed] [PMC]

285. Alaeddini M, Etemad-Moghadam S. SARS-Cov-2 infection in cancer patients, susceptibility, outcome and care. Am J Med Sci. 2022;364:511–20. [DOI] [PubMed] [PMC]
286. El-Arif G, Farhat A, Khazaal S, Annweiler C, Kovacic H, Wu Y, et al. The Renin-Angiotensin System: A Key Role in SARS-CoV-2-Induced COVID-19. Molecules. 2021;26:6945. [DOI] [PubMed] [PMC]
287. Farahani M, Niknam Z, Mohammadi Amirabad L, Amiri-Dashatan N, Koushki M, Nemati M, et al. Molecular pathways involved in COVID-19 and potential pathway-based therapeutic targets. Biomed Pharmacother. 2022;145:112420. [DOI] [PubMed] [PMC]
288. Babu M, Snyder M. Multi-Omics Profiling for Health. Mol Cell Proteomics. 2023;22:100561. [DOI] [PubMed] [PMC]
289. Wang X, Fan D, Yang Y, Gimple RC, Zhou S. Integrative multi-omics approaches to explore immune cell functions: Challenges and opportunities. iScience. 2023;26:106359. [DOI] [PubMed] [PMC]
290. Anawade PA, Sharma D, Gahane S. A Comprehensive Review on Exploring the Impact of Telemedicine on Healthcare Accessibility. Cureus. 2024;16:e55996. [DOI] [PubMed] [PMC]
291. Llanos AAM, Ashrafi A, Ghosh N, Tsui J, Lin Y, Fong AJ, et al. Evaluation of Inequities in Cancer Treatment Delay or Discontinuation Following SARS-CoV-2 Infection. JAMA Netw Open. 2023;6:e2251165. [DOI] [PubMed] [PMC]