Cancer research in Lebanon: Scope of the most recent publications of an academic institution (Review)

SAMAH TAWIL[1] and NADA KHADDAGE-SOBOH[2]

[1]School of Medicine; [2]Adnan Kassar School of Business, Lebanese American University, Beirut 1102 2801, Lebanon

Abstract. Cancer may be considered one of the most interesting areas of study, and although oncology research has grown markedly over the last decade, there is as yet no known cure for cancer. The objective of the present review is to examine various approaches to cancer research from a single institution, summarize their key conclusions and offer recommendations for future evaluations. The review examined 72 cancer-associated studies that were published within six years from 2017 to 2022. Published works in the subject fields of 'cancer' or 'oncology' and 'research' that were indexed in Scopus and Web of Science were retrieved and sorted according to article title, author names, author count, citation count and key words. After screening, a total of 28 *in vitro*/animal studies and 46 patient-associated published studies were obtained. A large proportion of these studies comprised literature reviews (20/72), while 20 studies were observational in nature. The 72 publications included 23 in which various types of cancer were examined, while the remaining studies focused on specific types of cancer, including lung, breast, colon and brain cancer. These studies aimed to investigate the incidence, prevalence, treatment and prevention mechanisms associated with cancer. Despite the existence of extensive cancer research, scientists seldom contemplate an ultimate cure for cancer. However, it is crucial to continuously pursue research on cancer prevention and treatment in order to enhance the effectiveness and minimize potential side effects of cancer therapy.

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1. Introduction

Cancer poses an important global public health challenge and ranks as the second leading cause of death worldwide, following heart diseases. The American Association of Cancer Research states that the primary objective of the study of cancer is the development of safe and effective approaches for the prevention, detection, diagnosis, treatment and cure of this disease (1). Advancing the understanding of cancer, including its treatment options, preventive measures and psychological impact, is crucial for making substantial progress in the reduction of its profound human and economic toll on the well-being of patients. Enormous sums of money have been spent on cancer research worldwide (2). However, due to extensive exposure to numerous environmental chemicals in everyday life and the complex nature of chemical mixtures (3), it is challenging for long-term safety evaluations to provide perpetual true results concerning cancer diagnosis and treatment as well as accurate updates. An ultimate cure for cancer remains the top aim of numerous researchers (4). Despite the marked increase in cancer research and the substantial growth in the number of cancer survivors over the past three decades, it is undeniable that the global occurrence of this disease continues to rise (5). Regarding cancer survival, it has been reported that during the last decade half of the individuals diagnosed with cancer in England survived their disease for ≥10 years (6). While there have been numerous advancements in the pharmacological treatments of tumors, and new highly sensitive techniques for the early diagnosis of pathologies, including imaging, laboratory tests, tumor biopsy, endoscopic examination, surgery, genetic testing and microfluidic systems have been developed (7,8), a definite cure for cancer remains elusive. Nevertheless, researchers persist in their efforts to develop new and more effective treatments and preventive measures for cancer. For example, long-term epidemiological studies have identified specific risk factors, such as the maintenance of a healthy weight, avoidance of tobacco, limitation

Correspondence to: Dr Samah Tawil, School of Medicine, Lebanese American University, P.O. Box 13-5053, Chouran, Beirut 1102 2801, Lebanon
E-mail: samah.tawil@lau.edu

of alcohol intake and protection of the skin that, if reduced, can prevent the development of certain types of cancers (9,10). Moreover, cancer risk prediction models based on these epidemiologic data have identified the risk of an individual carrying a genetic mutation for a specific cancer, such as BRCA 1 and/or BRCA 2 (11). Additionally, several innovative treatments, including hormonal therapy, monoclonal antibodies and chimeric antigen receptor T-cell therapy (12), are already being used alongside more traditional cancer therapies. Research efforts are now particularly focused on the role of gene editing and nanoparticles in combating cancer cells (13). Furthermore, a recent breakthrough in our understanding of the regulatory functions of small RNAs, originally discovered in plants, is providing new insights into the biology of cancer (14). Despite the clear rational and contemporary interest in cancer research, its assessment comes with challenges. Firstly, despite the recent surge in interest, there remains a lack of knowledge regarding the most effective methods for conducting research assessments (15). Secondly, in 2020, updates on the diagnosis and treatment of cancer were negatively impacted by the coronavirus disease (COVID)-19 pandemic. Restrictive measures and the closure of healthcare settings during the pandemic led to limited access to care, resulting in delays to cancer diagnosis, treatment and research updates regarding cancer incidence and etiologies (16). In Lebanon, particularly at the Lebanese American University (LAU), several scientific studies were conducted to explore new cancer therapies and preventive measures (17-20). However, according to a 2021 report from the Global Cancer Observatory of the National Cancer Registry, there were 11,589 new cancer cases and 6,438 cancer-related deaths in Lebanon in 2020 (21). One notable finding is the absence of data on the survival rate of cancer cases in the official Lebanese registry maintained by the Lebanese Ministry of Public Health (22).

Hence, the objectives of the present review are to examine cancer research methodologies documented in LAU libraries, with a particular focus on publications following the outbreak of COVID-19, assess these methodologies, consolidate their key findings and provide recommendations for future assessments. The present study encompasses various aspects of cancer research, including fundamental laboratory investigations and human studies, as well as basic scientific and applied research. It encompasses research pertaining to pediatric or adult cancer, as well as studies spanning the nursing, medical and public health aspects of cancer research. Consequently, the study seeks to achieve the following: i) Identify existing literature reviews that document approaches to the assessment of research impact and summarize these approaches; ii) summarize the findings of each study based on different cancer types; and iii) make recommendations to steer future cancer research towards addressing the specific requirements of the Lebanese population.

2. Study retrieval

The present study focused on the analysis of publications from the LAU (Beirut, Lebanon) over the past 5 years, specifically from 2017 to 2022. These publications were selected as a representative sample of a Middle Eastern academic and medical research center. During this time period, the School

of Pharmacy and the School of Medicine at LAU actively participated in cancer research, conducted studies and stayed up-to-date with the latest advancements. The dataset used for analysis was obtained from SciVal (https://librairies.lau. edu.lb/research/databases/?index=S#id_libdbform), a research performance assessment tool that facilitates the analysis of data from Scopus and Web of Science (WOS). While there were variations in coverage between these two indices, the present study considered articles that appeared in both to provide a broader perspective on the correlation between citation count and author number. The study of published cancer research at LAU is based on the collaborative efforts between academic researchers and medical physicians. The search was initiated under 'all subject areas' and then proceeded using specific themes such as 'medicine' and 'cancer research'. Published works were also extracted with specific keywords such as 'neo*', 'tumor', 'cancer', 'oncol*', 'leukem*', 'lymph*', 'chemo*' and 'radio*' as individual topics. The search in the category 'institutions and groups' was limited to 'The Lebanese American University'; Lebanon was the country of choice in the category 'countries/regions' and the date limits were '2017-2022'. The data obtained from SciVal included i) article title, ii) author names, iii) author count, iv) citation count, v) field-weighted citation impact, and vi) CiteScore (CS). Bibliometric analysis was performed to compare the published works in the present study. In order to achieve this objective, the CS was used as the primary method for counting citations (23,24). The present review only included published articles and focused exclusively on peer-reviewed journals, even though the selection of journals may vary depending on the citation-based metric system being considered, resulting in different quartiles. No restrictions were made regarding author names and collaborations. Additionally, single- and hyper-authored publications, abstracts only, studies written in a language other than English, corrections to previous studies, errata, conference proceedings and book series were excluded.

Nearly all the published research from the specified years were included in the present study. To ensure accuracy and relevance, two independent reviewers conducted a thorough screening of all records based on the topic search. The screening process involved reviewing study titles for potential relevance to cancer research and examining the full-text articles for specific references to cancer.

3. Study design and setting

Between 2017 and 2022, a total of 2,137 research works by LAU were published in journals indexed in Scopus and WOS, covering various research fields. Out of these, 252 studies specifically focused on cancer research. Following the PRISMA guidelines, a thorough screening process was conducted based on the titles and abstracts of the publications as depicted in Fig. 1. After removing duplicates, corrections and errata, 124 papers remained for full-text review. Ultimately, 72 studies were deemed eligible and met the inclusion criteria. The number of publications gradually increased from 2017 until 2021, reaching its peak in 2020, when 26.3% of the studies were published and remained constant in 2021. However, the number of papers published dropped in 2022 (Fig. 2), comprising only 8.3% of the studies in this time
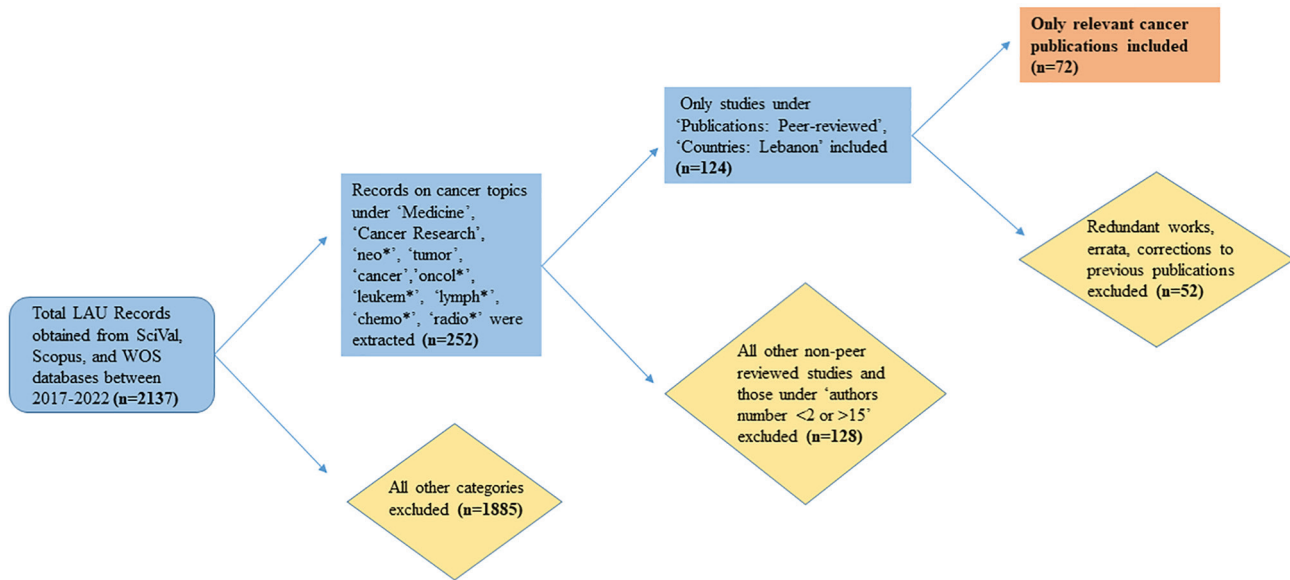
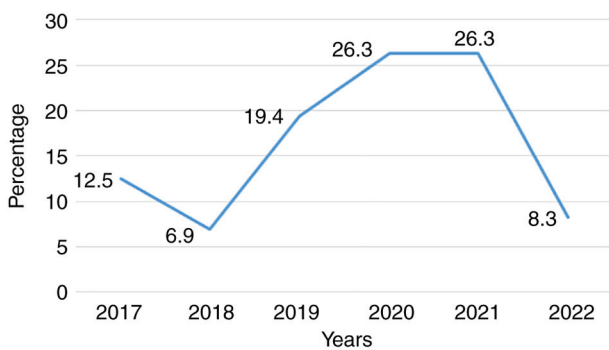Figure 1. Diagram of the study selection process. LAU, Lebanese American University; WOS, Web of Science.

Figure 2. Percentage of cancer-associated publications per year.

period. Among the 72 publications, 25 focused on *in vitro* or animal studies, while 47 were patient-associated studies.

Considering the patient-associated studies, the highest proportion were literature reviews (18/72), followed by 5 systematic reviews, 1 meta-analysis and 22 observational studies of a cross-sectional, cohort or case-control nature. In addition, there was one interventional randomized controlled study. Fig. 3 provides an overview of the types of cancer studies reported by the LAU directory. Notably, two studies specifically targeted fetal cancer and metastasis, and involved pregnant women. Furthermore, five studies were conducted on the pediatric population.

4. Types of cancer and main endpoint

The faculty at LAU conducted research on various types of cancer. Some of these studies specifically investigated new herbal treatments and examined their anticancer properties (7/72 publications). In total, 28 of the 72 publications examined multiple cancer types or cancer in general. The primary objectives of these studies were twofold: Firstly, to explore pharmacological mechanisms and highlight pathways for cancer prevention (39.1%); and secondly, to evaluate the

psychological challenges associated with cancer (30.4%). One study specifically focused on the identification of potential risk factors associated with cancer (5). The remaining studies each focused on specific types of cancer, such as lung, breast, colon or brain cancer. The main objectives of these studies were to investigate the incidence, prevalence, treatment options and prevention mechanisms for these specific types of cancer. Studies that focused on understanding the regulatory functions of small RNAs and human recombinant arginase I in the treatment of cancer constituted only 4.16% of all publications and were all published in 2020 (25-27). Additionally, several *in vitro* studies were conducted, which examined either a variety of cancer types or specific types of cancer. More comprehensive information on the various types of cancer researched is presented in Fig. 4.

5. Detailed description of LAU cancer studies

In the LAU dataset of 72 cancer publications, 38.89% covered all types of cancer, as indicated in Table I (18,28-53), while the remaining 61.11% focused on specific oncological types, as shown in Table II (10,17,19,20,25-27,54-90). These two tables provide additional information about each study, including its main focus, aim/purpose, study type, the type of cancer studied and key findings. Moreover, Figs. 5 and 6 depict the trends of cancer studies in terms of study types and types of cancer, respectively, across the years.

6. Principal findings

The aim of the present investigation was to assess the quantity and quality of cancer studies reported by the LAU and explore their respective objectives and areas of focus. The review encompasses *in vitro*, *in vivo* and animal studies. A relatively high number of literature reviews and a prevalence of observational studies over experimental ones were conducted. This finding may be expected since observational studies are generally easier to perform, more convenient and less stringent
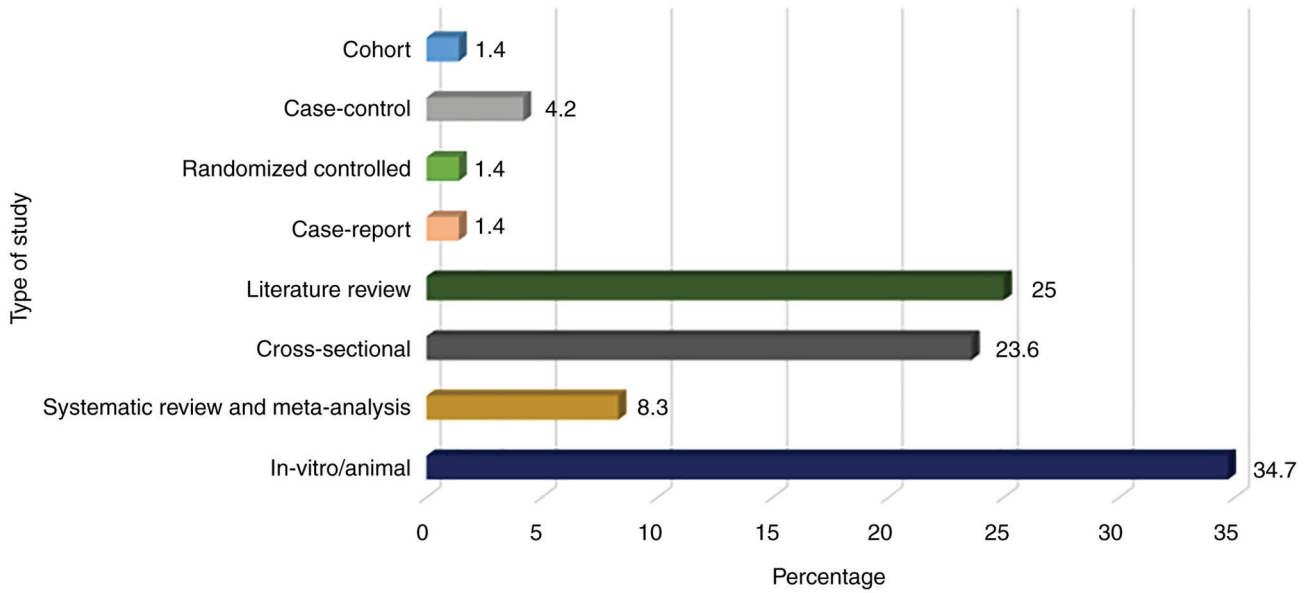
Figure 3. Types of studies included in the Lebanese American University research directory between 2017 and 2022.
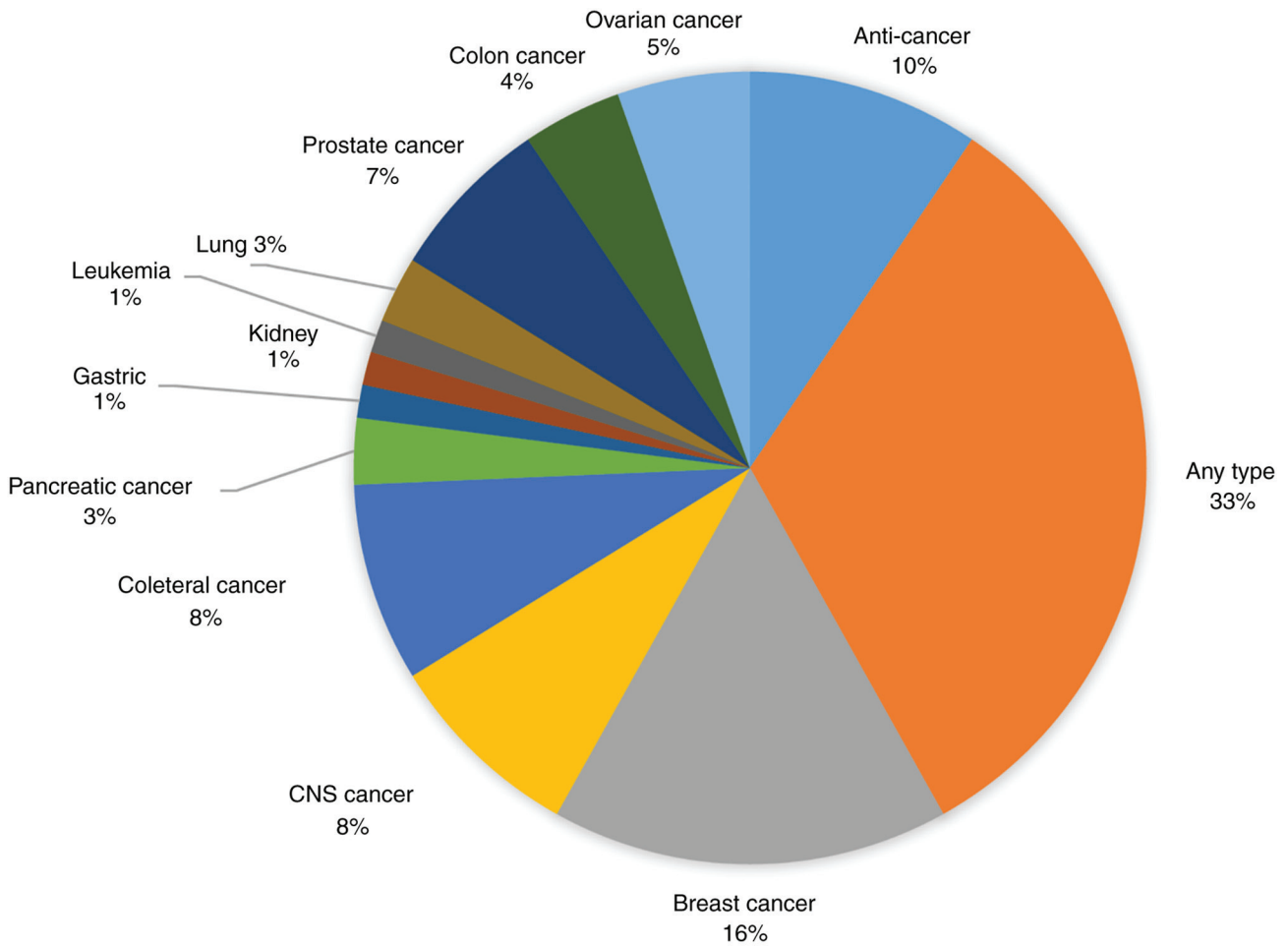
Figure 4. Types of cancer studied at the Lebanese American University between 2017 and 2022.

compared with interventional studies, although they carry a lower level of evidence (91).

The aims of the included studies varied, and in some cases it appeared that the main objective was solely descriptive. Therefore, it is essential to conduct more interventional, experimental and well-controlled human studies that possess higher external validity and generalizability. Such studies would lead to more definitive conclusions and trustworthy recommendations (92).

Table I. Publications on miscellaneous types of cancer according to study type and date of publication.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Khazzaka et al, 2022	Systematic review	Incidence/ occurrence/ risk factors		Examination of the literature concerning placental and fetal metastases among pregnant women with cancer via the identification of clinical and pathological characteristics, treatment trends and prognosis	Fetal metastasis occurred mainly in patients with placental metastases derived from melanoma and lung cancer primaries and was associated with a dismal prognosis	(28)
Atat et al, 2022	Literature review	Anticancer updates	NA	Explain the importance of 3D culture in representing the tumor microenvironment as well as the effects of 3D cancer cells on the behavior, resistance, proliferation and metastasis of cancer	3D systems are currently used for disease modeling and pre-clinical drug testing	(29)
Sacca et al, 2022	Cross-sectional	Qualitative	Observational	Evaluation of patient trust predictors when seeking cancer-related information from doctors and the internet	The role of confidence in seeking cancer-related information consistently influences the levels of trust attributed to each source of information	(30)
Karam et al, 2021	In vitro animal	MOA	NA	Evaluation of the targeted effect of parthenolide in vitro and in animals, after extensive experiments targeting its anti-inflammatory and anticancer properties	Supports the use of parthenolide and urges further clinical development	(31)
Hoteit et al, 2021	Literature review	Anticancer updates	NA	Explain the immune-based mechanisms used in tumor cell proliferation and maintenance, as well as the rationale behind various treatment methods	Immunotherapy used alone or in combination with various types of therapeutics has potential in cancer treatment	(32)
Jaafar et al, 2021	In vitro	Safety	NA	Collection of ambient particle-bound polycyclic aromatic hydrocarbons (PAH)	Three major sources were found to contribute to PAH emissions at the urban	(33)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
				in three Lebanese coastal cities and investigation of their cancer risk	background site, namely, traffic (48%), diesel generators (23%), and incineration (29%). The cancer risk was found higher than what was measured at the same site in previous years with an increase of 35%	
Chaftari et al, 2021	Cross-sectional	Mortality	Observational	Use of C-reactive protein, procalcitonin and lactate biomarkers of sepsis to create a prediction model for short-term mortality in patients with cancer and suspected infection	A simple new scoring system for mortality prediction, based on readily available clinical and laboratory data, including procalcitonin, C-reactive protein and lactate was developed that can be used in emergency departments for patients with cancer and suspected infection	(34)
Massoud et al, 2021	Cross-sectional	Qualitative/ opinion	Observational	Evaluation of the healthy lifestyle practices recommended by hematologists/oncologists for patients during treatment. Correlational analysis between the hematologists/oncologists' sociodemographics and the lifestyle recommendations they provided to patients	Communication gaps between hematologists/ oncologists and patients with cancer should be addressed, and solutions to identified barriers should be implemented to achieve higher quality patient-centered care	(35)
Alrubai et al, 2022	Cross-sectional	Qualitative/ opinion	Observational	Assessment of the psychological health status, depression, anxiety and stress levels of patients with cancer in Iraq during the COVID-19	Findings including the association between the development of new pain and depression, raised concerns regarding the	(36)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
				pandemic, and the relationship between such factors and sociodemographic characteristics	psychological health of patients diagnosed with cancer during the COVID-19 pandemic	
Khaled et al, 2021	Cross-sectional	Validation	Observational	Validation of the EPIC FFQ in Lebanon	EPIC FFQ can be considered a valid tool for the assessment of diet in epidemiological studies among Lebanese adults	(37)
Al-Koussa et al, 2020	Literature review	MOA	NA	Discussion of different arginine deprivation agents and their mechanism of action, stressing the factors that affect cell migration and the effect of arginine on metastases via polyamines	De novo arginine synthesis is not sufficient to compensate for the high nutritional requirements of cancer cells, forcing them to rely on an extracellular supply of arginine	(38)
Diab et al, 2020	Literature review	MOA	NA	Explain the roles of CDK7 in cancer cells and provide an overview of the pharmacophores of CDK7 inhibitors, their efficacy in various cancer models and clinical development	CDK7 is uniquely involved in the transcription regulation and cell cycle progression in many types of cancer. CDK7 inhibitors have demonstrated a promising profile of safety with lowgrade side effects, and regimens against various advanced solid tumors are in place to assess their clinical efficacy as a single agent and in combination.	(39)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Bechnak et al, 2020	In vitro	MOA	NA	Study of the cytotoxicity of curcumin-based colloidal nanocapsules and investigation of whether anticancer activity is enhanced by curcumin encapsulation	A375 cells treated with the curcumin colloidal nanocapsules showed a significant increase in single- and/or double-strand DNA breaks upon exposure to light, indicating promising biological effects	(40)
Hrusak et al, 2020	Cross-sectional	Incidence/ occurrence/ risk factors	Observational	Investigation of COVID-19 incidence and severity among children on anticancer treatment through a survey distributed virtually over 25 countries	Children receiving anticancer chemotherapy may have a mild or asymptomatic course of COVID-19. While the risk of developing a more severe course of COVID-19 should not be underestimated, the intensity of preventive measures should not cause delays or obstructions to oncological treatment	(41)
Nassour et al, 2020	Systematic review	Anti-cancer updates/ waste	NA	Systematic review of anticancer drugs in the aquatic environment	Significant heterogeneity within methodologies made it challenging to compare results and draw conclusions. Nevertheless, the study aids the evaluation of proposed recommendations to guide future studies and reviews	(42)
Mehanna et al, 2020	In vitro	MOA	NA	Optimization and validation of a facile liquid chromatography-tandem mass spectrometry method to detect and quantify three	The method was advantageous compared with prototypical inductively coupled plasma-mass	(43)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
				Ru(II) polypyridyl complexes in cells, plasma and urine	spectrometry-based techniques *in vitro* and *in vivo*, which anticipates its utilization in cellular uptake, pharmacokinetics and pharmacodynamics studies	
Assi *et al*, 2020	Literature review	MOA	NA	Discussion of the major resistance patterns and outcomes associated with the use of prior targeted therapies in two oncological solid tumors	Collaborative efforts at the molecular level are advancing the design of improved drugs or combinatorial strategies and the development of more sensitive assays to monitor responses and resistance	(44)
El Baba *et al*, 2020	Literature review	MOA	NA	Evaluation of how Rho GTPases regulate VEGF signaling and the outcomes of this interaction on the progression of cancer	The Rho GTPases are among the most important molecules for signal transduction in cancer cells. They regulate cytoskeleton remodeling, proliferation, and migration among others. VEGF controls angiogenesis and vascular permeability of endothelial cells and acts downstream of Rho GTPase-related signaling. The role of Rho GTPases, in the regulation of angiogenesis by modulating the expression of VEGF or regulating tube formation has been well established	(45)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Elias *et al*, 2019	*In vitro*	MOA	NA	Isolation of *Cedrus libani* extract 7-HC and investigation of its anticancer and antiinflammatory activities	7-HC possesses promising anticancer and anti-inflammatory activities, and may serve as a lead molecule in cancer therapy	(18)
Doumit *et al*, 2019	Cross sectional	Qualitative/ opinion	Observational	Exploration of spirituality and its positive effect on the family caregivers of children with cancer in Lebanon	As the first study in the Middle East to address the meaning of spirituality in this population, may pave the way for a customized palliative care program and integrative approach to patient care	(46)
Bar-Sela *et al*, 2019	Cross sectional	Qualitative/ opinion	Observational	Study of the barriers to staff providing spiritual care to patients, based on the observation that decreased usage of aggressive treatments at the end of life occurs when patients feel spiritually supported. Analyzed a subgroup of physicians and nurses whose inclination to provide improved spiritual care provision was unrealized	Despite relatively high levels of spiritual care provision, there is a gap between desirability and actual provision due to certain barriers, such as inadequate training of healthcare professionals and lack of space for appropriate discussions	(47)
Hageh *et al*, 2018	*In vitro*	MOA	NA	Investigation of a series of sterically encumbered Cu(I) bis-phenanthroline complexes for use in PCT	The photocytotoxicity of these long-lived cuprous phenanthroline complexes was successfully demonstrated, suggesting that this class of photosensitizers may be exploited for PCT applications	(48)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Moghnieh et al, 2017	Literature review	Guidelines/ updates	NA	Provide guidelines on the management of infections in patients with febrile neutropenia in an era of rising antimicrobial resistance, devised by panel members on behalf of the Lebanese Society of Infectious Diseases and Clinical Microbiology. These are expected to support care providers by providing standardized care processes	Various factors play a role in the management of febrile neutropenia in patients with cancer, including local microbiology epidemiology and the availability of diagnostic tests and antimicrobial agents	(49)
Doumit and Khoury, 2017	Cross-sectional	Qualitative/ opinion	Observational	Investigation of the factors facilitating and hindering the coping methods of Lebanese parents of a child with cancer	The enabling factors were social/family support; talking about it; strong religious beliefs; and the communication style of health workers. On the other hand, the deterring factors were the waiting time and the hospital stay; changes in the couple's relationship; and sibling rivalry. Nursing and medical staff need to be conscious of parents' coping strategies and their impact on family dynamics and the relationship between the family and the health care team.	(50)

Table I. Continued.

First author/s, year	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Razik et al, 2017	In vitro/ animal	MOA	NA	Synthesis of two series of new purine bioisosteres comprising a pyrazol (3,4-d)pyrimidine scaffold linked to piperazine moiety through different amide linkages and evaluation of their anticancer activity	Certain pyrazolopyrimidine derivatives possessed in vitro anti-inflammatory and anticancer activities	(51)
Liu et al, 2021	Literature review	MOA	NA	Review of the roles of divalent metal ions in the inhibition of IDH, their role in the tricarboxylic acid cycle and the associated metabolism	Demonstrates the importance of substrate-metal ion complexes in R132H IDH1 catalysis and the basis for selective R132H IDH1 inhibition	(52)
Bar-Sela et al, 2019	Cross-sectional	Qualitative/ opinion	Observational	Survey of physicians and surgeons from the Middle East to investigate the linkage between attitudes to spiritual care and the spiritual care of patients with cancer	Development level of a country is a key factor influencing attitudes toward spiritual care and its actual provision	(53)
Assi et al, 2020	Cross sectional	Qualitative/ opinion	Observational	Assessment of whether molecular profiling helps physicians in therapeutic decision making via the analysis of molecular profiles of cancer after the failure of at least one standard-of-care treatment using NGS, IHC and other tests	NGS combined with IHC/other tests provides useful information for aiding the treatment decisions of oncologists in routine clinical practice	(44)

3D, 3-dimensional; NA, not applicable; MOA, mechanism of action; COVID, coronavirus disease; EPIC FFQ, European Prospective Investigation into Cancer Food Frequency Questionnaire; VEGF, vascular endothelial growth factor; 7-HC, 7-himachalen-7-ol; PCT, photochemotherapy; IDH, isocitrate dehydrogenase; NGS, next-generation sequencing; IHC, immunohistochemistry.

Table II. Publications on specific cancer types according to study type and date of publication.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Jayaraj et al, 2020	Prostate	Systematic review/ meta-analysis	MOA	NA	Systematic review and meta-analysis of the theragnostic effects of miRNA and the utility of miRNAs as clinical theragnostic biomarkers	The expression of specific miRNAs as theragnostic biomarkers in medical oncology was suggested	(25)
Khalife et al, 2020	Breast	Literature review	MOA	NA	Review of miRNAs involved in BC, highlighting their effect on drug and therapy resistance	Specific miRNAs were shown to be up- or downregulated in BC	(26)
Elias-Rizk et al, 2020	Breast	Cross-sectional	MOA	Observational	Evaluation of various lncRNA H19 threshold levels in normal vs. proliferative and malignant tissues, and investigation of the link between such levels and BC classification	LncRNA H19 could be a potential marker for BC diagnosis, prognosis and risk management	(27)
Chemaly et al, 2022	Gastric	Systematic review	Incidence/ occurrence/ risk factor	NA	Comparative analysis of data on gastroesophageal cancer occurrence after gastric bypass procedures	Gastroesophageal cancers after gastric bypass procedures occur commonly in the excluded stomach where many are not identified by conventional means	(54)
Assouad et al, 2022	Kidney	Cross-sectional	Incidence	Observational	Analysis of kidney cancer occurrence in Lebanon over 12 years and a comparative analysis with other countries	Lebanon presented an average-to-high ASR for kidney cancer compared with other countries in its region, but a below-average ASR compared with countries worldwide	(55)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Swayden *et al*, 2021	Colorectal	*In vitro*	MOA	NA	Testing the therapeutic potential of targeting colon cancer cells via arginine deprivation induced by HuArgI(Co)-PEG5000	Colon cancer cells are partially auxotrophic for arginine and sensitive to HuArgI(Co)-PEG5000-induced arginine deprivation Activation of autophagy is not protective, but induces cytotoxicity and leads to cell death	(56)
Nader *et al*, 2021	Breast	Case report	Safety	Observational	Description of a case of immune-mediated encaphalitis and a literature review of the neurological immune-related adverse events associated with various checkpoint inhibitors	Early recognition of the side effects and their treatment is crucial	(57)
Chatila *et al*, 2021	Colorectal	Cross-sectional	Incidence/ occurrence/ demographics	Observational	Demographical description of Lebanese patients with CRC. The method of detection, age of onset, stage at presentation, treatment modalities and survival rate are detailed	Lebanese patients affected by CRC tend to present with advanced disease stages, leading to poor prognosis and survival	(10)
El-Mais *et al*, 2021	Pancreatic	*In vitro*	MOA	NA	Examination of the effects of arginine depletion induced by HuArgI(Co)-PEG5000 on PANC-1 cell migration, adhesion and invasion	HuArgI (Co)-PEG5000 shows promising results for arginine depletion in the treatment of pancreatic cancer cells	(58)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
El-Saghir et al, 2021	Breast	Literature review	Qualitative/ opinion	NA	Explorative commentary presenting the challenges of oncologists in the diagnosis and management of BC with BRCA gene mutations in Lebanon and the Middle East	Genetic counseling, continuing education, infrastructure, testing, expertise and financial support are required to fulfill unmet needs in the management of BRCA mutation carriers	(17)
Khater and Abou-Antoun, 2021	CNS	Literature review	Anticancer updates	NA	Elaboration of the interventions that may contribute to the clinical therapeutic resistance observed in pediatric CNS tumors during medical trials of c-Met targeting agents	Potential mechanisms include the overexpression and activation of compensatory tumorigenic mechanisms within the tumors or ineffective drug delivery methods	(59)
Atallah et al, 2021	Ovarian	Cross-sectional	Incidence/ occurrence/ risk factors	Observational	Testing the rate, repartition and risk factors of lymph node metastasis in patients with epithelial ovarian cancer	Serous histology, grade 3 tumors, positive peritoneal cytology, advanced clinical stage, interval surgery and bilateral adnexal involvement predict lymph node metastasis in patients with epithelial ovarian cancer	(60)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
El-Chami et al, 2021	Breast	In vitro	MOA	NA	Evaluation of the effect of LeTx on the migration, adhesion and invasion of BC cells, and its potential mechanism involving the dysregulation of the Rho GTPases RhoA and Cdc42	LeTx treatment reduced the migration, adhesion and invasion of BC cells, and this effect was associated with the dysregulation of RhoA and Cdc42	(61)
Hilal et al, 2021	Colorectal	Cross sectional	Survival	Observational	Comparative study of rectal cancer tumor characteristics and outcomes in patients older or younger than 40 years in a Lebanese institution	In younger patients a worse disease-free survival and evidence of an association between younger age at diagnosis and poor outcomes was observed, suggesting that the personalized upfront intensification of treatment should be considered in the young	(62)
Jaafar et al, 2021	Prostate	In vitro	MAO	NA	Evaluation of the role of StarD13 and how it targets and interacts with cancer molecules	StarD13 acts as a tumor suppressor that inhibits the invasion of PCa cells	(63)
Fayad et al, 2021	Lung and breast	In vitro	MAO	NA	Investigation of the photochemistry and effect of four strained photoactivatable polypyridyl ruthenium(II) complexes on A549 NSCLC and MDA-MB-231 triple negative BC cells	Complex C3 was observed to be a promising selective photoactivatable chemotherapeutic agent that induces reactive oxygen species production and apoptosis	(64)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
Bahmad et al, 2021	CNS	In vitro	MOA	NA	Testing the potential antitumor effect of tideglusib on three human neuroblastoma cell lines, SK-N-SH, SH-SY5Y and IMR-32	Tideglusib targeted neuroblastoma CSCs, thereby overcoming therapy resistance	(19)
Khalil and Abi-Habib, 2020	Pancreatic	In vitro	MOA	NA	Evaluation of the sensitivity of pancreatic cancer cells to HuArgI(Co)-PEG5000-induced arginine deprivation and the mechanisms underlying deprivation-induced cell death	Pancreatic cancer cells are auxotrophic for arginine and sensitive to HuArgI(Co)-PEG5000-induced arginine deprivation	(65)
Idriss et al, 2020	Breast	In vitro	MOA	NA	Investigation of the antiproliferative effects and pro-apoptotic mechanisms of β-T3 on the human breast adenocarcinoma cell lines MDA-MB-231 and MCF7	Vitamin E family member β-T3 is as a promising anticancer agent that is more effective than γ-T3 for the treatment of human BC	(66)
Nasreddine et al, 2020	Ovarian	In vitro	MOA	NA	Assessment of arginine auxotrophy in ovarian cancer cells through the induction of arginine deprivation by HuArgI(Co)-PEG5000	Activation of autophagy following arginine-deprivation, is not protective and mediates cell cytotoxicity leading to death by autophagy	(67)
Bahmad et al, 2020	CNS	Literature review	Anticancer updates	NA	Summary of drug repurposing methodologies adopted to cure pediatric brain tumors and discussion of compilation	Drug repurposing or repositioning is a promising approach for the identification of novel therapeutic	(68)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
					approaches that may elevate drug repurposing to an advanced level	strategies to target brain tumors and overcome therapy resistance	(20)
Tfayli et al, 2020	Lung	Randomized controlled	Treatment	Interventional	Assessment of the benefits of immune checkpoint inhibitors in the neoadjuvant therapy of patients with early-stage NSCLC	The addition of immunotherapy to chemotherapy did not appear to enhance the overall response rate in patients with resectable NSCLC in the neoadjuvant setting as the study failed to meet its primary endpoint	
Joumaa et al, 2020	Colorectal	In vitro/ animal	MOA	NA	Testing the effect of aqueous chamomile extract against DMH-induced CRC in mice	Chamomile acts as a potent dietary chemopreventive agent against DMH-induced CRC	(69)
Tannous et al, 2020	Leukemia	In vitro	MOA	NA	Investigation of the potential anticancer effect of the flaxseed lignans secoisolariciresinol diglucoside, enterodiol and ENL on AML cells in vitro and the underlying molecular mechanism	ENL exerts promising anticancer effects on AML cell lines in vitro, by promoting DNA fragmentation and the intrinsic apoptotic pathway, highlighting the protective health benefits of flax seeds in leukemia	(70)
Younes et al, 2020	Breast	In vitro	MOA	NA	Evaluation of the potential anticancer activity of AELE in vitro in MDA-MB-231 and MCF-7 BC	AELE exhibits a selective antiproliferative and pro-apoptotic	(71)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/interventional	Aim/purpose	Main finding	(Refs.)
					cell lines, and determination of the toxicity level in normal mesenchymal stem cells	effect on chemo-resistant MDA-MB-231 BC cells, providing evidence for the antitumor effects of *A. cherimola*	
Ghali *et al*, 2019	Breast	Case-control	Incidence/ occurrence/ risk factors	Observational	Exploration of the contribution of NF-κB variants to the pathogenesis of BC in a Middle Eastern-North African population	Reveals the positive association of rs3774937 with BC	(72)
Bahmad *et al*, 2019	CNS	Literature review	MOA	NA	Summary of the key molecules in neuroblastoma CSCs	Experimental evidence from neuroblastoma cell lines, patient-derived xenografts and primary tumors is presented	(73)
Al-Koussa *et al*, 2019	Colorectal	*In vitro*	MOA	NA	Testing the cytotoxic effect of HuArgI(Co)-PEG5000 on the CRC cell lines HT-29, Caco-2 and Sw837	Arginine depletion is a potential selective approach for inhibiting the motility and invasion of CRC cells	(74)
Henaine *et al*, 2019	Colorectal	Cohort	Anticancer treatment	Observational	Evaluation of the clinical effectiveness of targeted therapy in patients with metastatic CRC in Lebanese oncologic units and an estimation of the costs	Targeted therapy associated with standard therapy is highly prevalent in Lebanon in metastatic disease and the associated medical cost is substantial	(75)
Cianci *et al*, 2019	Ovarian	Systematic review	Incidence/ occurrence/ risk factors	NA	Review of evidence describing the association of sarcopenia with	Sarcopenia appears to have an important role in the	(76)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
					surgical and oncological outcomes in patients with ovarian cancer	oncological outcomes of patients with ovarian cancer	(77)
Najem et al, 2019	Colorectal	In vitro	MOA	NA	Evaluation of the effect of SAHA, a pan-histone deacetylase inhibitor and/or DAC, a DNA methyltransferase inhibitor, on the Caco-2 human colon cancer cell line in vitro	Profound antitumorigenic effects of sequentially combined SAHA and DAC were found in the CRC cell line and new insights into the corresponding molecular mechanism were obtained	(78)
El-Amm and Aragon-Ching, 2019	Prostate	Literature review	Anticancer updates	NA	Reviews the pivotal clinical trials that supported the approval of apalutamide and enzalutamide in the non-nmCRPC setting as well as the main potential and challenges of these agents	Apalutamide and enzalutamide are new anti-androgen treatment options in the nmCRPC setting	(79)
Hoter et al, or 2019	Prostate	Literature review	MOA	NA	Reviews the functions and role of HSPs in PCa progression	HSPs may have a role in PCa progression and it is necessary to further evaluate the approach of HSP inhibition as a cancer treatment strategy	(80)
Al Saud et al, 2018	Breast	Systematic review	Safety	NA	Explanation of the flap sensory reinnervation mechanism	Zoster reactivation in breast reconstructed patients objectively	

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
					of the reconstructed breast based on clinical findings, and provision of a diagnostic and management algorithm for zosteriform rash in patients with breast cancer	demonstrates reinnervation of the skin flap	
Bedoui *et al*, 2018	Colorectal	Case-control	Incidence/ occurrence/ risk factors	Observational	Investigation of the association of six IL-17A gene variants (rs3819024, rs2275913, rs3819025, rs10484879, rs7747909 and rs3748067) with CRC susceptibility in a Tunisian population	IL-17A rs10484879 single nucleotide polymorphism and IL-17A haplotypes AGGTG and GAGTG constitute independent factors for CRC susceptibility. IL-17A may be a target for future CRC immunotherapy	(81)
Ghali *et al*, 2018	Breast	Case-control	Incidence/ occurrence/ risk factors	Observational	Evaluation of the relationships among estrogen receptor ESR1 and ESR2 variants, breast cancer and associated features in Tunisian women	ESR1 alleles and genotypes, and specific 3-locus ESR1 haplotypes are associated with increased breast cancer susceptibility in Tunisian women. However, the ESR2 variant and specific 1-locus ESR1 haplotype have a protective effect	(82)
Al Hassan *et al*, 2018	CNS	*In vitro*	MOA	NA	Investigation of the anti-invasive antimetastatic effect of metformin on	Metformin demonstrates anti-invasive antimetastatic potential. There was a	(83)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
					glioblastoma multiforme and its mechanism of action	significant decrease in the survival of SF268 cancer cells in response to treatment with metformin. Furthermore, metformin's efficiency in inhibiting 2D cell motility and cell invasion in addition to increasing cellular adhesion was also demonstrated in SF268 and U87 cells	
Nader et al, 2018	Prostate	Literature review	Anti-cancer updates	NA	Provision of a historical summary and explanation of the contemporary use of chemotherapeutic agents in PCa in various states and phases of the disease	Promising results in locally advanced PCa and high-risk PCa have been obtained in the neoadjuvant and adjuvant settings	(84)
Daaboul et al, 2017	Colorectal	In vitro/ animal	MOA	NA	Investigation of the anticancer activity of Daucus carota oil extract HC against SW1116 colon cancer cell lines, and evaluation its effect in a DMH-induced colon carcinogenesis model in black 6 mice	Low dose HC treatment induced cell cycle arrest and promoted apoptosis via inhibition of the MAPK/ERK and PI3K/AKT pathways. HC treatment exerted an antitumor effect in vivo with no significant toxicity to the mice	(85)
Abou-Antoun et al, 2017	CNS	Literature review	Anti-cancer updates	NA	Review of the progress in CSC biology and its	CSC-targeting approaches in	(86)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
					association with targeted therapies that may clearly differ between pediatric and adult brain tumors	combination with current clinical therapies have the potential to be more effective owing to their ability to compromise CSC maintenance	
Najar et al, 2017	Breast	In vitro	MOA	NA	Investigation of the role of bone marrow-derived MSCs in the mediation of selective bone metastasis by BC cells	MSCs strongly contribute to the adaptation and invasiveness of BC cells in skeletal tissues	(87)
Salem et al, 2017	Breast	Cross-sectional	Diagnosis	Observational	Analysis of the breast mammogram density distribution in Lebanese women and its correlation with BC incidence	Breast density distribution in Lebanon is similar to that in western society. Also, similar to other studies, it showed that high breast density is statistically associated with BC, particularly in older and menopausal women	(88)
El-Amm et al, 2017	Prostate	Literature review	Anticancer updates	NA	Examination of the companion PROs in conjunction with abiraterone acetate use, as PROs are increasingly considered as a key metric for drug label claims when regulatory agencies grant approval	Abiraterone has shown benefits in the second- and first-line (post- and pre-chemotherapy) settings, with improvements in overall survival and secondary end points such as PSA and radiographic	(89)

Table II. Continued.

Study	Cancer type	Study type	Main focus	Observational/ interventional	Aim/purpose	Main finding	(Refs.)
						response rates, time to PSA progression and progression-free survival	
Shebaby et al, 2017	Skin	In vitro/ animal	MOA	NA	Examination of the cytotoxic effect of Daucus carota oil fractions on human epidermal keratinocytes and the chemopreventive activity of the pentane diethyl ether fraction on DMBA/TPA-induced skin carcinogenesis in mice	The F2 fraction exhibited marked antitumor activity against DMBA/ TPA-induced skin carcinogenesis, possibly mediated through inhibition of the MAPK/ERK and PI3K/AKT pathways	(90)

NA, not applicable; ASR, age-standardized rate; MOA, mechanism of action; HuArgI (Co)-PEG5000, pegylated cobalt-substituted recombinant human arginase I; CRC, colorectal cancer; BC, breast cancer; CNS, central nervous system; LeTx, anthrax lethal toxin; PCa, prostate cancer; NSCLC, non-small cell lung cancer; CSCs, cancer stem cells; T3, tocotrioenol; miRNA, microRNA; DMH, 1,2-dimethyl hydrazine; ENL, enterolactone; AML, acute myeloid leukemia; lncRNA long non-coding RNA; AELE, Annona cherimola ethanolic leaf extract; SAHA, suberoylanilide hydroxamic acid; DAC, decitabine; nmCRPC, metastatic castration-resistant PCa; HSP, heat shock protein; IL, interleukin; HC, β-2-himachalen-6-ol; MSCs, mesenchymal stromal cells; PROs, patient-related outcomes; PSA, prostate-specific antigen; DMBA, dimethylbenzanthracene; TPA, tetradecanoylphorbol acetate.
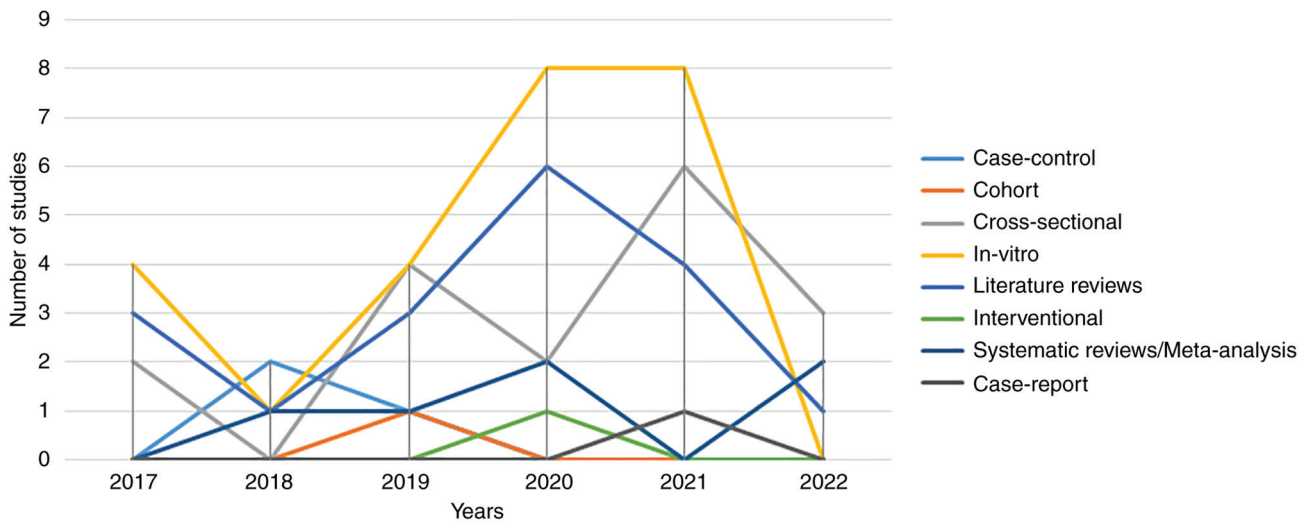
Figure 5. Cancer study types at the Lebanese American University between 2017 and 2022.
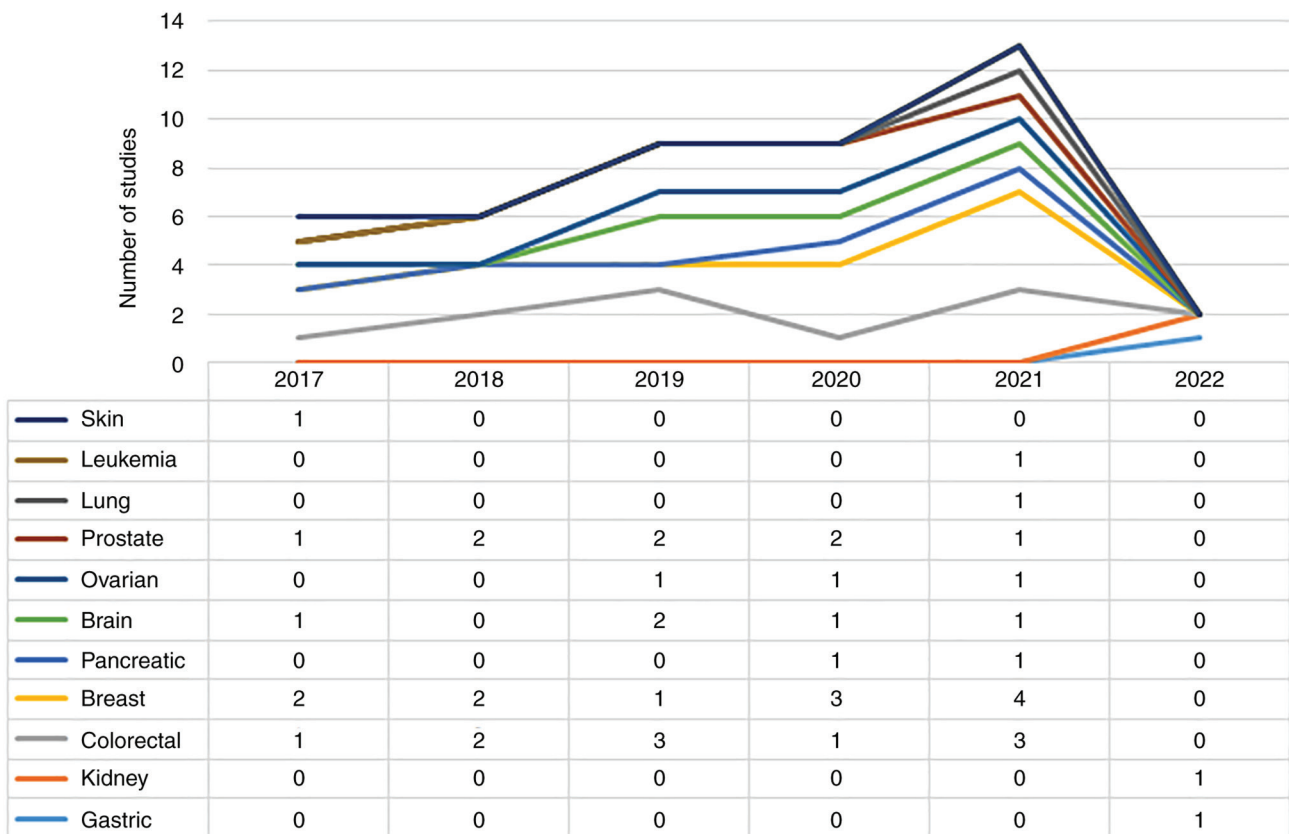

	2017	2018	2019	2020	2021	2022
Skin	1	0	0	0	0	0
Leukemia	0	0	0	0	1	0
Lung	0	0	0	0	1	0
Prostate	1	2	2	2	1	0
Ovarian	0	0	1	1	1	0
Brain	1	0	2	1	1	0
Pancreatic	0	0	0	1	1	0
Breast	2	2	1	3	4	0
Colorectal	1	2	3	1	3	0
Kidney	0	0	0	0	0	1
Gastric	0	0	0	0	0	1

Figure 6. Different types of cancer studied at the Lebanese American University between 2017 and 2022.

The present analysis reveals that researchers at the LAU who are interested in cancer have focused on a variety of research areas. The most common type of study involved laboratory experiments, namely *in vitro* studies, which accounted for more than one-third of the LAU studies. Animal models are important tools in cancer research *in vitro* and *in vivo*, as they can be used in the identification of carcinogens, development of cancer therapies and drug screening, and for providing insights into the molecular mechanisms of tumor growth and metastasis (93). In addition, they are easy to manipulate,

homogenous, accessible and do not require human participants (94). The latter point was highlighted in the present study, which showed that this type of study was most prevalent during 2020-2021, during the era of COVID-19.

Special updates and reviews on novel anticancer therapies were also shown to be prevalent in the present study. Notably, these findings, particularly those concerning the regulatory roles of small RNAs, have provided new insights to improve the global understanding of cancer biology. Although these types of studies were the most prevalent during the year 2020,

prior to the spread of COVID-19 and the economic crisis that impacted research funding negatively in Lebanon, in coming years, broader revelations about fundamental aspects of cellular biology are likely to increase our understanding of the aberrant behavior of cancer cells and notably contribute to the advancement of biomedical research (14). In addition to anticancer treatment, other studies had additional objectives, such as determining the incidence and prevalence of specific types of cancer, identifying risk factors associated with certain cancers and exploring their socio-economic and psychological impacts. Indeed, the diverse range of findings from these studies on cancer underscores the broad spectrum of interest of researchers to this field and emphasizes the requirement for well-balanced, patient-centric research strategies that can yield improved outcomes and higher cure rates (95).

Just a few decades ago, clinical investigators and physicians were often advised to refrain from engaging in oncology due to its complexity and the discouraging clinical outcomes it yielded. Additionally, conducting cancer research required significant financial investment and relied on patients dedicating their time and effort (96). Currently, the primary challenge lies in the development of fundamental research on cancer prevention and treatment to impede the occurrence of new cases and reduce the global incidence of cancer.

Although the annual output of cancer research appears to be low when compared with that of other publications on different research subjects, a sharp increase in the number of cancer publications was noticed during the years of 2018 and 2019 in the present study. This underlines the increased involvement of LAU scholars in research as the aim of expanding the number of publications and citations, as well as the support offered by the academic institution as an incentive, seems to have had a positive impact on the publication rate of papers on cancer. In fact, Boutros and Fakih (97) argued in their recent publication that the number of academic publications was associated with academic promotion across all institutional settings. The authors also concluded that the positive consequences of the number of publications of each faculty member suggests that this factor should be a priority for administrators to consider when making decisions regarding promotion. LAU is a leading private and nonsectarian higher education institution that operates under a charter from the Board of Regents of the University of the State of New York, and has a large publication volume relative to its faculty size, which makes it an ideal source of relevant information (98). In terms of quality, LAU provides incentives for researchers to publish their studies in the top 10% of international journals; thus, LAU is a research-active institution of higher learning in Lebanon and the region, with no compromise in its commitment to quality teaching (99). Moreover, the urgency of conducting cancer research has escalated due to the high prevalence of cancer worldwide, with approximately one in two individuals receiving a cancer diagnosis in their lifetime (100). Despite current treatments, cancer-associated mortality and morbidity rates remain high (6). This global situation mirrors the situation in Lebanon, as indicated by the 2021 report from the Global Cancer Observatory of the National Cancer Registry, which revealed an increase in cancer cases despite ongoing research on cancer (22). As a result, oncological research has garnered public funding and global monetary investments to incentivize clinical investigators to pursue cancer research (101).

Despite the aforementioned increase in cancer-associated publications, a reduction in the number of publications was observed in 2021. A possible explanation for this is the outbreak of the novel COVID-19 that has impacted all types of research in various forms (102,103). Another potential explanation is the lack of funds required for research in general imposed by the severe socio-economic Lebanese crisis and political instability manifested by unprecedented rates of unemployment, inflation and poverty, and a rapid devaluation of the Lebanese currency since the beginning of 2021 (104,105).

Research on breast and colorectal cancer was found to be the most prevalent among that on all types of cancer, accounting for >30% of all cancer studies. This finding is not unexpected since, according to previous studies, these types of cancer were the most prevalent in Lebanon during the last 5 years (22,106). Unfortunately, research on breast and colorectal cancers decreased in 2022 since Lebanon was continuing to face a serious economic crisis with an effect on fiscal and human resources.

Reflecting upon the approaches to cancer research outlined in the present study, it is necessary to highlight several further recommendations. First, it is essential to conduct more research using real-life data in order to accurately assess the actual impact of research on cancer incidence, treatment, outcomes and prevention techniques. Additionally, there is a requirement for more clinical studies involving the users and beneficiaries of cancer research, such as patients and their families. It would be beneficial for these studies to involve a greater representation of individuals from real-world populations, with the development of a prospective study plan to establish specific targets for trial enrolment based on disease epidemiology and incidence. Moreover, it is crucial to allocate more robust, sustained and predictable funding for additional clinical and translational longitudinal molecular profiling studies in large and diverse cohorts of patients with cancer. This will aid in understanding the natural progression of cancers and exploring the role of biology and genetics in cancer health disparities. Furthermore, the national public health workforce should prioritize cancer control initiatives that aim to reduce the incidence, morbidity and mortality of cancer. These initiatives may also focus on improving the quality of life for individuals with cancer by implementing evidence-based interventions for prevention, early detection, diagnosis and treatment. Additionally, it is important to develop well-planned strategies to guide future cancer research.

7. Significance of the study and future implications for policy and practice

The issue of cancer research studies being underrepresented or misrepresented is an important factor contributing to therapy delays and proactive measures are required to address this. The importance of the present review lies in its summary of the different cancer studies that were conducted in an academic university during a 5-year period. The review has shown that cancer research is an attractive topic for many academic researchers; however, the spread

of COVID-19 and the economic crisis had a major impact on this type of research, which might have contributed to a shift in study types towards more observational or *in vitro* studies as well as a remarkable reduction in research output, particularly after the spread of COVID-19 in 2020. From this perspective, it is essential to emphasize that researchers must re-focus their efforts on conducting studies associated with cancer, since cancer research should be recognized as one of the most prevalent health concerns, as is COVID-19. To develop new therapies, gain a deeper understanding of cancer prognosis and survivorship and ensure the availability of new drugs in all healthcare settings, a collaborative effort involving the diverse cancer research community in each country is necessary. Translational cancer research, particularly interventional or experimental human studies, is recommended to be an integral part of the delivery of oncology care, ensuring that valuable knowledge is gained in academic institutions and nationally. For this reason, policy proposals should be made to enhance access to digital healthcare, expand healthcare programs, allocate funds for experimental cancer research and provide financial support to healthcare institutions. Moreover, interventional studies that focus on anticancer therapy should be the primary interest of pharmaceutical companies as well as research centers since, according to the present results, only a few of these were conducted.

It is important to emphasize that the impact of cancer research can be amplified when organizations use a multidisciplinary approach, as demonstrated by the diversity of studies in the present review, which can guide and enhance future evaluations.

8. Conclusions

At present, scientists seldom contemplate an ultimate cure for cancer. However, further research on the short-term and long-term effects of current cancer therapies is necessary. For instance, efforts can be made to address the psychological and socioeconomic challenges faced by cancer patients during their treatment, or to find methods of mitigating the potential side effects experienced during therapy. By combining technological advancements with ongoing operational research, the field of oncology will be able to move on from the era when surgery and chemotherapy were the sole treatment options available.

Availability of data and materials

Not applicable.

Authors' contributions

NKS wrote the literature review, was responsible for the methodology and organized the findings. ST collected and analyzed data, designed and guided the study, and drafted and critically revised the final version of the manuscript. Data authentication is not applicable. Both authors have read and confirmed the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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