

Economics of Pediatric Cancer in Four Eastern Mediterranean Countries: A Comparative Assessment

Adrian Gheorghe, PhD¹; Kalipso Chalkidou, PhD^{1,2}; Omar Shamieh, MD³; Tezer Kutluk, MD, PhD⁴; Fouad Fouad, MD⁵; Iyad Sultan, MD⁶; and Richard Sullivan, MD⁷

PURPOSE Cancer is a leading cause of death among children in the Eastern Mediterranean region, where conflict and economic downturn place additional burden on the health sector. In this context, using economic evidence to inform policy decisions is crucial for maximizing health outcomes from available resources. We summarized the available evidence on the economics of pediatric cancer in Jordan, Lebanon, the occupied Palestinian territory, and Turkey.

METHODS A scoping review was performed of seven academic databases and gray literature pertaining to pediatric cancer in the four jurisdictions, published between January 1, 2010, and July 17, 2019. Information was extracted and organized using an analytical framework that synthesizes economic information on four dimensions: the context of the health system, the economics of health care inputs, the economics of service provision, and the economic consequences of disease.

RESULTS Most of the economic evidence available across the four jurisdictions pertains to the availability of health care inputs (ie, drugs, human resources, cancer registration data, and treatment protocols) and individual-level outcomes (either clinical or health-related quality of life). We identified little evidence on the efficiency or quality of health care inputs and of pediatric cancer services. Moreover, we identified no studies examining the cost-effectiveness of any intervention, program, or treatment protocol. Evidence on the economic consequences of pediatric cancer on families and the society at large was predominantly qualitative.

CONCLUSION The available economic evidence on pediatric cancer care in the four countries is limited to resource availability and, to an extent, patient outcomes, with a substantial gap in information on drug quality, service provision efficiency, and cost-effectiveness. Links between researchers and policymakers must be strengthened if pediatric cancer spending decisions, and, ultimately, treatment outcomes, are to improve.

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INTRODUCTION

Globally, the burden of childhood cancer falls disproportionately on low- and middle-income countries.¹ In the Eastern Mediterranean region (EMR), with its young demographic profile, cancer is the third-leading cause of death (after injuries and violence) among children aged 5 to 14 years.² Most of what is known about the economics of childhood cancer is relatively recent, informed by data collected in high-income countries, and suggests there is much more to the subject than the direct cost of treatment. Indirect costs, including travel to and from hospitals, accommodation and loss of earnings, are at least as substantial as direct costs. Having a child with cancer who requires long-term (in some cases, up to 2 years) treatment may lead to job disruption, loss of income for both parents (particularly mothers), or even divorce—all of which bring about or accentuate financial hardship,

including selling assets, and affect lifestyle.³⁻⁵ Furthermore, children surviving cancer will grow into adulthood with substantially increased risk for a range of chronic conditions such as hearing loss and abnormal lung function as a result of therapy.⁶ At the same time, there appears to be little research on the comparative value of therapeutic strategies for childhood cancers.⁷

The relevance of these issues—cost-effectiveness, affordability, financial protection, quality of care, and long-term follow-up of survivors—is further exacerbated in health systems facing the consequences of conflict, political instability, severely constrained resources, and weak governance. In these contexts, economic evidence is even more important when informing the design and implementation of effective policy instruments (eg, cancer control plans, financing mechanisms, procurement systems).

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

To summarize the evidence on the economics of pediatric cancer in Jordan, Lebanon, the occupied Palestinian territory, and Turkey.

Knowledge Generated

Much more is known about the availability of inputs, such as medication, human resources, and registry data, than about how efficiently, effectively, cost-effectively, or equitably inputs are being converted into services and health outcomes. Some evidence gaps are common to all four settings, such as information on the financial protection implications of accessing cancer services, whereas others are unique to each setting.

Relevance

Improving the quality of pediatric cancer spending decisions in the region requires conducting detailed cost analyses of pediatric cancer interventions; investing in building or, if already available, auditing cancer registries; conducting cost-effectiveness analyses of tracer interventions; and establishing governance mechanisms that promote the production and use of (locally generated) evidence in decision-making.

In this study, we summarize the available evidence on economic aspects of pediatric cancer in four EMR countries to identify evidence gaps and research priorities. We focus on Jordan, Lebanon, the occupied Palestinian territory (OPT), and Turkey because these are focal countries of the Research for Health in Conflict in Middle East and North Africa project, which aims to build capacity for health research, including health economics and the political economy of health, in the region; these four countries also are the EMR's most significant hosting nations for children with cancer. Our expectation is that such a comprehensive review will be useful for researchers and decision makers with an interest in improving pediatric cancer care outcomes in the EMR.

METHODS

Analytical Framework

We distilled elements from several available frameworks exploring the economics of illness⁸⁻¹¹ into a framework that synthesizes economic information on four aspects: the context of the health system, the economics of health care inputs, the economics of service provision, and the economic consequences of disease (Table 1). Each domain comprises several dimensions with associated generic indicators. For example, the economics of health care inputs aspect comprises drugs, equipment, human resources, data, and treatment protocols.

Approach and Data Sources

We conducted a scoping review of the academic and gray literature pertaining to pediatric cancer in Jordan, Lebanon, OPT, and Turkey published between January 1, 2010, and July 17, 2019. We used a systematic literature search of eleven databases (Medline, Embase, Global Health, Health Management Information Consortium, PsycInfo, Scopus, Web of Science, Econlit, Index Medicus for the Eastern Mediterranean Region, and Centre for Reviews and Dissemination NHSEED and HTA databases). Full details of

the search strategy are listed in Appendix Table A1. We also searched the websites of the WHO and United Nations High Commissioner for Refugees (UNHCR) for additional reports or links to relevant information sources.

Analysis. Records were downloaded in Mendeley reference management software and screened by one researcher against the domains, dimensions, and generic indicators of the analytical framework. The themes and findings of relevant records were synthesized narratively and validated with academic experts in each country.

RESULTS

Context

Epidemiology. Every year, approximately 4,000 to 4,500 new pediatric cancer cases (children aged 0 to 14 years) are currently diagnosed in Turkey, Jordan, Lebanon, and the OPT combined (Table 2). The majority of pediatric cancer cases occur in Turkey, where crude and age- and sex-adjusted incidence rates (17.2 and 17.7 per 100,000, respectively¹²) are higher than in the other three countries and > 50% higher than the world averages (10.2 and 10.3 per 100,000, respectively). The proportion of new pediatric cancer cases relative to the total number of new cancer cases (all ages) varies significantly but is higher than the 1.1% to 1.2% global average. The top five cancer site distributions are comparable across the four populations and with global figures (Fig 1), except in Jordan, where the incidence of leukemia is slightly lower than in the other countries.

Some of these figures can be corroborated with registry data. For example, in Jordan, 245 new pediatric cancer cases were registered among Jordanian children in 2015, representing 4.4% of total new cancer cases.¹³ Estimates of incident cases among child refugees in the four countries are much sparser in the absence of comprehensive cancer surveillance programs and population-based registration. In Jordan, 178 cases were registered among non-Jordanian

TABLE 1. Framework Used to Analyze the Economic Dimensions of Pediatric Cancer

Health System Context	Health Care Inputs	Service Provision	Economic Consequences of Disease
Epidemiology: Incidence, prevalence, and DALYs	Drugs: Pricing, availability (formulary and actual), accessibility, and quality	Outcomes: Clinical outcomes and patient-reported outcomes	Impact on patients and care givers
Service provision: Number and distribution of pediatric cancer units, and mix of services available	Equipment: Availability, distribution, and use	Efficiency: Cost, service use, and intensity	Impact on society
Health financing: Funding and reimbursing pediatric cancer care costs	Human resources: Availability, knowledge, attitudes, and practices Data: Cancer registration, data completeness and quality Protocols: Availability and uptake	Cost-effectiveness of interventions and programs	Impact on health care providers

Abbreviation: DALY, disability-adjusted life year.

TABLE 2. Key Cancer Epidemiologic Indicators for Pediatric Cancer by Population Aged 0 to 14 Years²

Indicator	Jordan	Lebanon	Palestine	Turkey	Worldwide
GLOBOCAN 2018					
Incidence, cases	390	183	207	3,464	200,166
Incidence crude, per 100,000	11.2	13.3	10.4	17.2	10.2
Incidence ASR, per 100,000	11.3	13.4	10.5	17.7	10.3
Incidence, cases, all ages	10,898	17,294	4,499	210,537	18,078,957
Percent of incident cases, all ages	3.6	1.1	4.6	1.6	1.1
1-Year prevalence, cases	293	141	145	2,679	139,537
1-Year prevalence, per 100,000	8.4	10.3	7.3	13.3	7.1
5-Year prevalence, per 100,000	35.3	44.2	30.1	56.5	30.8
Global Burden of Disease 2017					
Incidence, cases	477	847	190	4,190	335,487
Incidence, cases, all ages	8,983	23,354	3,937	184,459	24,490,933
Percent of incident cases, all ages	5.3	3.6	4.8	2.3	1.4
1-Year prevalence, cases	4,339	13,129	1,745	41,139	5,142,327

Abbreviation: ASR, age-standardized rate.

child refugees in 2015¹³ and an estimated 62 new cancer cases occur among Syrian child refugees each year.¹⁴ In Turkey, there are reports of 212 cases treated between 2012 and 2015 at 17 centers in 10 cities,¹⁵ but these probably represent only a fraction of the total. Other estimates provide institutional perspectives; for example, 623 Syrian children received treatment at Ankara Child Health and Diseases Hospital between January 2016 and August 2017,¹⁶ and approximately 300 Syrian children received treatment at the Children's Cancer Center in Beirut.¹⁷

Service provision. Pediatric cancer care is provided in departments or units of generalist, cancer, or pediatric hospitals. In Lebanon, there are 14 hospitals with pediatric oncology departments, of which 11 are in Beirut and none are in Beqaa and South Lebanon provinces, where approximately half the Syrian refugees living in the country are located.¹⁷ Lebanon, however, hosts the only stand-alone pediatric cancer hospital in the four jurisdictions: Children's Cancer Center of Lebanon, which opened in 2002 and is hosted at the American University of Beirut

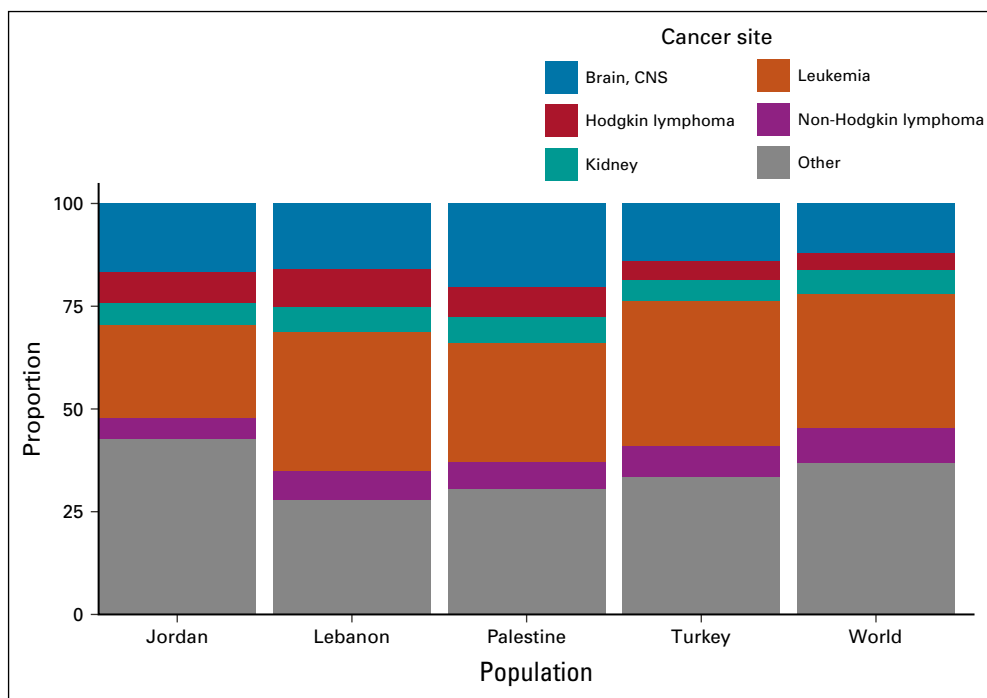


FIG 1. Distribution of incident cancer cases by population and cancer site (0-14 years). Source: GLOBOCAN estimates for 2019.¹²

in partnership with St Jude's Children's Hospital in Memphis, Tennessee.

In Jordan, pediatric cancer services are provided in the oncology departments of King Hussein Cancer Center (KHCC), which sees an estimated 80% of pediatric cancer cases nationally,¹⁴ and of the Royal Medical Services Pediatric Hospital, as well as the pediatric departments of King Abdullah University Hospital and Princess Rahma Hospital.¹⁹

In the OPT, cancer is the main reason for referral outside Ministry of Health facilities in both the West Bank and Gaza,²⁰ with Augusta Victoria Hospital in East Jerusalem being the main referral destination for patients with cancer and the only hospital in the OPT with a radiation facility. Patients needing to leave the West Bank or Gaza Strip for treatment face the hurdle of obtaining a permit from Israeli authorities, with a 61% average permit approval rate for patients with cancer, which is slightly higher than the average 54%. Huda Al Masri pediatric cancer department at Beit Jala Hospital and the Pediatric Oncology Unit of Al-Najah University in Nablus serve patients in the south and north parts of the West Bank, respectively. A pediatric oncology unit was recently established in the Gaza Strip by the Palestine's Children Relief Fund.

Regarding services other than cancer therapy (eg, palliative care, home care, long-term support), most sources refer to palliative care being underdeveloped.²¹⁻²³ Only one study explored in some depth potential barriers or challenges for palliative care: a survey of heads of 31 pediatric oncology units in Turkey reported the lack of professionals (58%), lack of physical space (48%), and lack of education (26%) among the perceived challenges to the development of palliative care.²⁴ We found one study reporting on the availability of services other than palliative care: a survey of 33 pediatric oncology departments in Turkey.²⁵ The authors found that only four units offered long-term follow-up of cancer survivors; the ones that did not invoked the lack of a survivorship clinic, insufficient education on survivorship, and busy work schedules.²⁵ KHCC appears to have the

most developed comprehensive pediatric palliative care in Jordan and the region, with inpatient and outpatient consultation service, inpatient hospice, and home care.²⁶

Financing. The health financing systems across the four jurisdictions have similarities and differences, as reflected by key indicators (Table 3). Although the extent to which health is a domestic spending priority, reflected in the proportion of domestic government health expenditure from general government expenditure, is comparable across the four settings (range, 10%-16%), health spending per capita (range, USD 257-645), population coverage with some form of insurance (range, 42%-99%), and the reliance on out-of-pocket payments (range, 16%-46% of current health expenditure) are markedly different. In Lebanon, in particular, the combination of high spending levels, low insurance coverage, and high out-of-pocket payments raises issues of protection against catastrophic health spending.

Cancer care is free for children in Jordan¹⁹ and Turkey.²⁷ In Lebanon, medicines for life-threatening diseases, including cancer, are provided for those without insurance coverage through an independent financing scheme overseen by the Ministry of Public Health (MOPH).²⁸ Private financing initiatives, such as Acute Support for Children and Adolescents in Lebanon, Amel Association International, and American Lebanese Syrian Associated Charities/St Jude Children's Research Hospital play an important role in fundraising to support access for refugee families who cannot afford treatment.

The situation of children with cancer who are Syrian refugees (as well as other migrant populations) is radically different across the four jurisdictions. In Turkey, the costs of cancer care for Syrian child refugees is covered by the government.²⁹ In Jordan, the government initially allowed Syrians registered with UNHCR to access health care services free of charge in Ministry of Health's facilities, but as of November 2014, Syrian refugees became required to pay the noninsured Jordanian rate for all types of health services in public facilities.¹⁴ On the other hand, the UNHCR selectively funds expensive treatments according

TABLE 3. Selected Health Financing Indicators in the Four Jurisdictions^{98,99}

Indicator	Jordan	Lebanon	Palestine	Turkey
Current health expenditure per capita (USD)	257	645	282	469
Domestic government health expenditure as percentage of current health expenditure	57	51	41	78
Domestic government health expenditure as percentage of gross domestic product	3.6	3.8	4.3	3
Domestic government health expenditure as percentage of general government expenditure	12	14	16	10
Out-of-pocket spending as percentage of current health expenditure	25	32	46	16
Estimated population covered by some form of public insurance, %	68	42	78.3	99.5

NOTE. All data are for 2015 except for "estimated population covered by some form of public insurance, which varies by country: 2015 for Jordan, 2017 for occupied Palestinian territory, unspecified for Lebanon. Data are for the entire health systems and not specific to pediatric cancer.

to the decision of the UNHCR Exceptional Care Committee. A previous study of the committee's decisions in Syria and Jordan between 2009 and 2012 showed that 48% of applications were funded, and the major reason for application denial was a determination of a poor prognosis.³⁰ More than two-thirds of Syrian children are covered through charity funds organized by the King Hussein Cancer Foundation for treatment at KHCC, where Syrian children receive the same treatment as Jordanian patients.

Economics of Health Care Inputs

Drugs. We could not identify any analysis that referred specifically to the availability, pricing, reimbursement, procurement, quality, or dispensing of drugs used in pediatric cancer in these four countries. However, we were able to construct a picture of the availability and accessibility for 10 of 19 anticancer drugs on the 2015 WHO Model List of Essential Medicines for Children,³¹ based on data collected throughout 2015 in a survey of 82 non-European countries, including Jordan, Lebanon, Palestine, and Turkey³² (Table 4). Although all 10 drugs are on the national drug lists of each of the four countries with full reimbursement (with the exception of cyclophosphamide tablets in OPT), some of them are not always available, particularly in Lebanon and Palestine, and the information is missing for Jordan. Barriers to accessibility differ by country: they tend to be manufacturing problems or lack of commercial motive in Turkey, budget restrictions in Palestine (for most cancer drugs), and no reliable supplier in Jordan. For Gaza, in particular, there are consistent reports of severe shortages of cancer drugs³³⁻³⁵ but no published systematic inventory.

We identified only one study directly comparing publicly listed prices for 22 anticancer drugs; the authors found prices in Lebanon tended to be among the lowest compared with the other eight countries (seven Asian countries and Egypt) in that study.³⁶ There are indications of cancer drug prices decreasing since 2011 in Lebanon, including through procurement negotiations led by the MOPH.³⁷ More recently, the government of Jordan reduced in June 2019 the list prices of > 1,000 drugs, including a 10% reduction for cancer drugs.³⁸ We did not identify any study examining the quality of drugs for pediatric cancer in the four countries reviewed in our study.

Equipment. We could not identify any systematic assessment regarding the availability, procurement processes, or use rates of therapeutic and diagnostic equipment in pediatric oncology units across the four jurisdictions. A global analysis underpinned by 2012 data found the available radiotherapy equipment in Jordan, Lebanon, and Turkey met the estimated demand for cancer care (at least at the time)³⁹; a previous analysis for the Lancet Oncology Commission also did not identify significant shortages in radiotherapy capacity.⁴⁰ In the Palestinian health sector, in 2014, three of 35 hospitals had

a magnetic resonance imaging scanner—all three were private hospitals.⁴¹

Human resources. A single study provided in-depth staffing information in pediatric oncology units. This was a 2012 survey of 31 pediatric oncology departments in Turkey that found all units had one or more pediatric oncology doctors and nurses, but only 26%, 13%, 7%, and 7% had a psychologist, social worker, psychiatrist, and physiotherapist, respectively.²⁴ Other sources provided only descriptive information or included only the total number of pediatric oncologists; for example, as of 2012, there were 15 pediatric oncologists working in Lebanon,²³ 20 in Jordan,¹⁹ and approximately 70 in Turkey.²⁷

Treatment protocols. We could not identify any source assessing which treatment protocols are used in pediatric oncology departments across each of the four jurisdictions. However, a number of clinical outcomes studies refer to the use of a range of international protocols, with or without adaptations, such as Berlin-Frankfurt-Munster,^{42,43} Children's Cancer Group, Children's Oncology Group,^{44,45} St Jude Total,^{46,47} National Wilms Tumor Study⁴⁸; or national protocols (eg, in Turkey).^{49,50} Turkey appears to be the only country in the sample where a national-level professional association (Turkish Pediatric Oncology Group) produces treatment protocols and guidelines, and conducts studies to assess their outcomes.

Cancer registration. A number of sources describe in some detail pediatric cancer registration in Turkey,^{51,52} Jordan,⁵³ and Palestine.⁵⁴ However, only the Palestinian source refers explicitly to the performance of cancer registration, specifically its fluctuations across space (eg, under-registration in selected districts) and time (eg, deficient leukemia registration between 2003 and 2005).

We found no studies attempting to estimate the extent of childhood cancer underdiagnosis or underreporting. However, a Turkish study examined the determinants of time to diagnosis (from contact with a health professional) and found longer time to diagnosis when the first contact was a nonpediatric specialist and much shorter as well as for infants and children older than 10 years.⁵⁵

Economics of Service Provision

Efficiency. We found no studies examining the efficiency or productivity of pediatric cancer services or facilities, but we identified three studies estimating the cost of specific pediatric cancer interventions. One Turkish study analyzed data from the national social security system for 148 pediatric cancer cases across five cancer types (Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, medulloblastoma, and osteosarcoma) and estimated an average cost of USD 25,045 per patient.⁵⁶ Two studies in Jordan estimated the average cost of chemotherapy for children with Ewing sarcoma⁵⁷ and of two L-asparaginase formulations for acute lymphoblastic leukemia (ALL),⁵⁸ respectively.

TABLE 4. Availability and Accessibility of Selected Anticancer Drugs on the 2015 WHO Model List of Essential Medicines in the Four Jurisdictions

Country	Formulary Availability and Patient-Facing Cost ^a				Actual Availability (accessibility with valid prescription)				Main Barrier to Accessibility ^b			
	Not on the Formulary	Missing Data	Partial Cost	Full Cost	Always	Usually or Half of the Time	Occasionally or Never	Missing Data	No or Unreliable Supplier	No Commercial Motive	Mfg Problems	Budget Capitation
Jordan	Trastuz	Anast	None	None	Unknown	Unknown	Unknown	All	Bleo CarboP CisP Cyclo (IV) Cyclo (tab) DTIC Dox Epir Etop ifos MTX VBL VCR	None	None	None
Lebanon	None	Capecit	< 25%:	None	CarboP	Anast	VBL	Capecit	None	None	None	Anast
						Bleo						
						CisP		Irino				Capecit
						DITC		Oxalipl				Oxalipl
						Docet		Imatinib				Paclit
						FU						Tam
						MTX (IV)						Trastuz
						Paclit						
						Dox						
						Epir						
						Etop						
						ifos						
						Trastuz						

(Continued on following page)

TABLE 4. Availability and Accessibility of Selected Anticancer Drugs on the 2015 WHO Model List of Essential Medicines in the Four Jurisdictions (Continued)

Country	Patient-Facing Cost ^a			Actual Availability (accessibility with valid prescription)			Main Barrier to Accessibility ^b					
	Not on the Formulary	Missing Data	Partial Cost	Full Cost	Always	Usually or Half of the Time	Occasionally or Never	Missing Data	No or Unreliable Supplier	No Commercial Motive	Mfg Problems	Budget Capitation
Palestine	Cyclo (tab)	None	None	None	Anast	Bleo Capecit	None	None	Oxalipl	Capecit	None	All others except;
						CarboP						Cyclo (tab)
					Docet	CisP						
						Cyclo						
						DTIC						
						Dox						Epir
						Etop						MTX (tab)
					Paclit	Ifos						Trastuz
						Irino						
						MTX (IV)						
						Oxalipl						
					Tam	VBL						
						VCR						
						Trastuz						
						Imatinib						
Turkey	None	None	None	None	All	None	None	None	FU	Bleo	Anast	None
										Cyclo		
										DTIC	Docet	
									Paclit	Etop	MTX (tab)	
									VBL	Ifos	Tam	
									VCR	MTX (IV)		

NOTE. Items in bold are on the 2015 WHO Model List of Essential Medicines for Children.³¹ Adapted from Cherny et al.³²

Abbreviations: Anast, anastrozole; Bleo, bleomycin; Capecit, capecitabine; CarboP, carboplatinum; CisP, cisplatinum; Cyclo, cyclophosphamide; DTIC, dacarbazine; Docet, docitaxel; Dox, doxorubicin; Epir, epirubicin; Etop, etoposide; FU, fluorouracil; Ifos, ifosfamide; Irino, irinotecan; IV, intravenous; Mfg, manufacturing; MTX, methotrexate; Oxalipl, oxaliplatinum; Paclit, paclitaxel; tab, tablet; Tam, tamoxifen; VBL, vinblastine; VCR, vincristine; Trastuz, trastuzumab.

^aAll drugs not listed are free.

^bDrugs not listed have no reported barrier.

Cost-effectiveness. We could not identify any full economic evaluation of a pediatric cancer health intervention or program.

Patient outcomes. We identified two nationwide analyses of survival after cancer treatment, both in Turkey. An analysis of data from 2002 to 2008 in the Turkish National Pediatric Cancer Registry found an overall 5-year survival rate of 65%,⁵² and a later analysis of the same registry (2009 to 2018 data) found an overall 5-year survival rate of 70.8%.⁵¹ Other studies were either conducted at a single hospital and/or focused on a single type of cancer. For example, in Turkey, studies focused on ALL,^{45,59} neuroblastoma,⁵⁰ rhabdomyosarcoma,⁶⁰ or Ewing sarcoma.⁶¹ In studies of data from Jordan, a 3-year overall survival rate of 75% was reported for all pediatric cancer types at King Hussein Cancer Center⁶² including ALL⁶³ and CNS tumors⁶⁴. Study data from Lebanon focused on osteosarcoma⁴⁴ and Ewing sarcoma.⁶⁵ Most studies concluded that the reported survival rates were generally lower but nevertheless comparable to those observed in high-income countries.

We could find only one study that applied a generic health-related quality-of-life instrument, namely the Short Form Survey-36, to evaluate the quality of life of children with cancer and their parents in Turkey. According to the study findings, they had affected health status relative to control subjects.⁶⁶ Other studies documented the quality of life of children undergoing cancer treatment,⁶⁷⁻⁷⁰ of parents and caregivers,^{18,71} and of child survivors.^{72,73} Many more studies examined the psychometric properties of various disease-specific instruments, particularly in Turkey, such as the KINDL scale,⁷⁴ Quality of Life and FAMCARE scales among caregivers,⁷⁵ Children's International Mucositis Evaluation Scale,⁷⁶ or the Adolescent Pediatric Pain Tool⁷⁷; and Jordan, including the Pediatric Quality of Life Inventory (PedsQL) Generic Core Scale, PedsQL Family Impact Scale, and the PedsQL Healthcare Satisfaction Hematology/Oncology Scale.⁷⁸

Economic Consequences of Disease

Economic burden on health service providers and the health care system. We identified one study protocol referring specifically to the costs of pediatric cancer care, and that was in Jordan.⁷⁹ Other sources referred to the overall financial burden of cancer care, for example, from the perspective of the Lebanese MOPH (cancer drugs cost USD 140 million over 3 years³⁶); but the way the data were presented did not allow disaggregation.

Economic burden on individuals, care givers, and families. Although a number of sources mentioned the financial burden of cancer care for parents and families (eg, in relation to the cost of chemotherapy drugs in Lebanon²³) or the relationship between financial concerns and measures of well-being,⁸⁰⁻⁸² we identified a single study that attempted to quantify this burden (n = 85 parents or care givers) on a scale from 1 (low) to 10 (high) and reported an

average score of 5.35 (standard deviation, 2.60), suggesting moderate financial hardship.⁸³ One qualitative study in Jordan, informed by interviews with 12 mothers and 12 fathers of children with cancer, documented what some Jordanian families may experience in terms of financial burden (eg, losing work, transportation, hotel costs).¹⁸ We found no study that quantified the volume of out-of-pocket payments, prevalence and distribution of coping mechanisms, or impact on job loss and job productivity.

Summary of Findings

Our main findings are summarized narratively in Table 5. Across the four countries, most of the available economic evidence pertains to the availability of health care inputs (ie, drugs, human resources, cancer registration data, and treatment protocols) and, to an extent, individual-level outcomes, either clinical or health-related quality of life. We identified little evidence on the efficiency or quality of inputs of pediatric cancer services; also, we identified no studies that examined the cost-effectiveness of an intervention, program, or treatment protocol. There was also limited information, most of it qualitative, on the economic consequences of pediatric cancer on families and the society at large.

Interpretation of Findings

Our findings point toward substantial gaps in the available economic evidence on pediatric cancer in all four countries. Some of these gaps are common to all, such as information on cost-effectiveness or implications for financial protection, whereas others are unique to each setting—for example, the availability and prices of cancer drugs in Jordan.

Explaining the evidence gaps is not straightforward, because several factors may be at play simultaneously. One may be a reluctance to engage with pediatric cancer from an economic perspective, given the relatively small number of cases (up to 5% of new cancer cases), the moral imperative of realizing children's right to health, and the risk of any economic argument being construed as rationing or cost cutting. Indeed, it can be counterargued that leaving economics out of the picture can easily lead to suboptimal decisions that deprive unseen patients of care they could have received. This counterargument is at the heart of framing childhood cancer care within the universal health care agenda.

The misalignment between research and policy priorities, reflected in the absence of coherent health research strategies in the region,⁸⁴ may also explain the gaps. The immediate example is drug pricing. Despite limited evidence on drug prices and their impact on the affordability of cancer care (to third-party payers and families) or efficiency of service delivery in general, the governments of Lebanon and Jordan have directed their attention to the issue over the past years and reduced list prices, presumably in response to perceiving drug prices as major cost drivers.

TABLE 5. Summary of Available Economic Evidence on Pediatric Cancer in the Four Countries

Country	Health Care Inputs	Service Provision	Economic Consequences of Disease
Jordan	<p>Drugs: Global study reports on formulary availability and main barrier to accessibility (no/unreliable supplier), but missing data on actual availability</p> <p>Limited evidence on equipment and old data on human resources (2012)</p> <p>No evidence on quality and completeness of registry data</p> <p>Limited evidence on protocol availability, uptake, and clinical effectiveness</p>	<p>Some evidence on clinical and patient-reported outcomes, including for survivors</p> <p>Institutional unit cost estimates (two studies at KHCC), no evidence on other measures of service use efficiency</p> <p>No evidence on cost-effectiveness of interventions and programs</p>	<p>Limited qualitative data on financial impact on parents and care givers. No evidence on the economic impact on society or health care providers</p>
Lebanon	<p>Drugs: Global study reports on formulary and actual availability, and main barriers to accessibility (budget capitation); several local studies on cancer drug prices</p> <p>No evidence on equipment and old data on human resources (2012)</p> <p>No evidence on quality and completeness of registry data</p> <p>Some evidence on protocol availability, uptake, and clinical effectiveness</p>	<p>Some evidence on clinical and patient-reported outcomes, including for survivors</p> <p>Institutional unit cost estimates (one source: CCI), no evidence on other measures of service use efficiency</p>	<p>Limited qualitative data on financial impact on parents and care givers. No evidence on the economic impact on society or health care providers</p>
Palestine	<p>Drugs: Global study reports on formulary and actual availability, and main barriers to accessibility (budget capitation)</p> <p>No evidence on equipment and human resources</p> <p>Some evidence on quality and completeness of registry data</p> <p>No evidence on protocol availability or uptake</p>	<p>No evidence on outcomes, efficiency, or cost-effectiveness</p>	<p>No data on financial impact on parents and care givers. No evidence on the economic impact on society or health care providers</p>
Turkey	<p>Drugs: Global study reports on formulary and actual availability, and main barriers to accessibility (commercial motive)</p> <p>No evidence on equipment and some evidence on human resources</p> <p>Extensive evidence on protocol availability, uptake, and clinical effectiveness</p>	<p>Extensive evidence on clinical and patient-reported outcomes, including for survivors</p> <p>Some evidence (one national study) on unit costs or other measures of service provision efficiency</p> <p>No evidence on cost-effectiveness of interventions and programs</p>	<p>No data on financial impact on parents and care givers. No evidence on the economic impact on society or health care providers</p>

Abbreviations: CCI, Children's Cancer Institute at the American University of Beirut Medical Center; KHCC, King Hussein Cancer Center, Amman, Jordan.

There is also the issue of limited capacity for health economics in the four countries, EMR and the Middle East and North Africa more broadly, which may have prevented health economics analyses from being conducted. Previous research programs, such as Research Capacity for Public Health in the Mediterranean, have tried to address this,⁸⁵ but much more is to be done.

Implications for Research and Policy

For researchers and policymakers, our findings point to the importance of local economic evidence to generate context-specific insights, particularly in the context of action for progress toward universal health coverage: Although some evidence is available and can be used already (eg, on specific barriers to cancer drugs accessibility), a substantial amount of information on current pediatric cancer provision is lacking, particularly on the main drivers of the cost of care, quantitative measures of family-level financial impacts, and cost-effectiveness of treatment protocols. This precludes making informed decisions on how to expand coverage and quality of care in the context of the WHO Global Initiative on Childhood Cancer⁸⁶ and the 2017 World Health Assembly resolution on cancer.⁸⁷

We propose four areas for additional consideration with associated recommendations:

1. **Costs:** Conduct detailed cost analyses of pediatric cancer services from the perspectives of providers and users as starting points for improving the quality, efficiency, and equity of cancer care provision. There is already evidence that quality cancer care can be delivered in low-resource settings at a fraction of the cost in high-income settings.⁸⁸
2. **Health outcomes:** Invest in building cancer registries and, where these are available, auditing and validating their data for pediatric cancers. There is evidence that accuracy of general cancer registries differs between adult and pediatric cancers because the latter usually constitute a more heterogeneous group.^{89,90}
3. **Cost-effectiveness:** Conduct pilot cost-effectiveness analyses of tracer interventions as the starting point for a multisectoral conversation on demonstrating and improving the value of cancer care. Initial analyses

can focus on small, well-defined units (eg, Tanzania,⁹¹ Mexico,⁹² El Salvador⁹³).

4. **Governance:** Establish a mechanism that promotes the production and use of evidence for cancer decisions by bringing knowledge producers, knowledge brokers, and knowledge users together. Such an example could be India's National Cancer Grid,⁹⁴ particularly for improving the quality of pathways and models of care. The costs (direct and indirect) of treating children with cancer need to be equitable, addressed by UNHCR and direct healthcare assistance to support host countries, particularly because pediatric oncology in refugee populations is an additional burden on health care systems beyond their own domestic populations. One aspect worth looking at is ensuring that reimbursement (at least from public funds) is tied to validated assays certifying the quality of anticancer drugs.

Strengths and Limitations

The main limitations of our analysis relate to the absence of a systematic assessment based on inclusion and exclusion criteria and the absence of a quality-assessment component; these were not attempted for practical reasons in light of our policy-facing objective and of the considerable difficulties raised by the wide range of economic topics surveyed, each with its methodological quality checklists. To our knowledge, this is the first analysis focused on the economics of pediatric cancer in the EMR and, for that matter, globally. It complements two previous analyses that either had a regional focus on cancer epidemiology in the general population,^{95,96} or a global focus on childhood cancer,¹ but neither included a discussion of economic implications.

In conclusion, the available economic evidence on pediatric cancer care in the four countries is largely limited to resource availability and, to an extent, patient outcomes, with a substantial gap in evidence for drug quality, service-provision efficiency, and cost-effectiveness. Links between researchers and policymakers must be strengthened to identify context-specific priorities for generating and using appropriate economic evidence that can improve pediatric cancer-spending decisions and, ultimately, treatment outcomes.

AFFILIATIONS

¹Global Health and Development, Imperial College London, London, United Kingdom

²Center for Global Development Europe, London, United Kingdom

³Center for Palliative and Cancer Care in Conflict, Department of Palliative Care, King Hussein Cancer Center, Amman, Jordan

⁴Department of Pediatric Oncology, Hacettepe University, Ankara, Turkey

⁵Faculty of Health Sciences, Global Health Institute, American University of Beirut, Beirut, Lebanon

⁶Department of Pediatric Oncology, King Hussein Cancer Center, Amman, Jordan

⁷Institute for Cancer Policy and Conflict & Health Research Group, King's College London, London, United Kingdom

CORRESPONDING AUTHOR

Adrian Gheorghe, PhD, Global Health and Development – Infectious Disease and Epidemiology, Imperial College London, St Mary's Campus, Norfolk Place, London W2 1PG, UK; Twitter: @adrianegheorghe, @r4hcmena; e-mail: a.gheorghe@imperial.ac.uk.

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AUTHOR CONTRIBUTIONS

Conception and design: Adrian Gheorghe, Kalipso Chalkidou, Richard Sullivan

Collection and assembly of data: All authors

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Agree to be accountable for all aspects of the work: All authors

otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/site/misc/authors.html.

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Richard Sullivan

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REFERENCES

- GBD 2017 Childhood Cancer Collaborators: The global burden of childhood and adolescent cancer in 2017: An analysis of the Global Burden of Disease Study 2017. *Lancet Oncol* 20:1211-1225, 2019
- Institute for Health Metrics and Evaluation, University of Washington: GBD Results Tool. <http://ghdx.healthdata.org/gbd-results-tool>
- Roser K, Erdmann F, Michel G, et al: The impact of childhood cancer on parents' socio-economic situation-a systematic review. *Psychooncology* 28:1207-1226, 2019
- Witte J, Mehlis K, Surmann B, et al: Methods for measuring financial toxicity after cancer diagnosis and treatment: A systematic review and its implications. *Ann Oncol* 30:1061-1070, 2019
- Tsimicalis A, Stevens B, Ungar WJ, et al: The cost of childhood cancer from the family's perspective: A critical review. *Pediatr Blood Cancer* 56:707-717, 2011
- Hudson MM, Ness KK, Gurney JG, et al: Clinical ascertainment of health outcomes among adults treated for childhood cancer. *JAMA* 309:2371-2381, 2013
- Russell HV, Panchal J, Vonville H, et al: Economic evaluation of pediatric cancer treatment: A systematic literature review. *Pediatrics* 131:e273-e287, 2013
- McDaid D, Sassi F, Merkur S, eds: Promoting Health, Preventing Disease. The Economic Case. 2015. http://www.euro.who.int/__data/assets/pdf_file/0006/283695/Promoting-Health-Preventing-Disease-Economic-Case.pdf?ua=1
- World Health Organization: WHO Guide to Identifying the Economic Consequences of Disease and Injury. Geneva, Switzerland, World Health Organization, 2009
- Cylus J, Papanicolas I, Smith P, eds: Health system efficiency: How to make measurement matter for policy and management. Copenhagen, Denmark: European Observatory on Health Systems and Policies, 2016
- Anand S, Desmond C, Fuje H, et al: The Cost of Inaction: Case Studies from Rwanda and Angola. Boston, MA, François-Xavier Bagnoud Center for Health and Human Rights, Harvard University, 2012
- International Agency for Research on Cancer: Global Cancer Observatory: Estimated number of new cases in 2018, all cancers, both sexes, ages 0-14. <https://gco.iarc.fr/today/home>
- Ministry of Health. Jordan Cancer Registry: Amman, Jordan, 2015. <https://www.moh.gov.jo/Pages/viewpage.aspx?pageID=414&keyword=cancer>
- Mansour A, Al-Omari A, Sultan I: Burden of cancer among Syrian refugees in Jordan. *J Glob Oncol* 4:1-6, 2018
- Kebudi R, Bayram I, Yagci-Kupeli B, et al: Refugee children with cancer in Turkey. *Lancet Oncol* 17:865-867, 2016
- Güngör A, Çatak Al, Çuhaci Çakir B, et al: Evaluation of Syrian refugees who received inpatient treatment in a tertiary pediatric hospital in Turkey between January 2016 and August 2017. *Int Health* 10:371-375, 2018
- Saab R, Jeha S, Khalifeh H, et al: Displaced children with cancer in Lebanon: A sustained response to an unprecedented crisis. *Cancer* 124:1464-1472, 2018
- Masa'Deh R, Collier J, Hall C: Parental stress when caring for a child with cancer in Jordan: A cross-sectional survey. *Health Qual Life Outcomes* 10:88, 2012
- Al-Rimawi HS: Pediatric oncology situation analysis (Jordan). *J Pediatr Hematol Oncol* 34:S15-S18, 2012 (Suppl 1)
- World Health Organization Regional Office for the Eastern Mediterranean. Right to Health: Crossing Barriers to Access Health in the Occupied Palestinian Territory 2017. Cairo, Egypt, World Health Organization, 2018
- Mojen LK, Rassouli M, Eshghi P, et al: Palliative care for children with cancer in the Middle East: A comparative study. *Indian J Palliat Care* 23:379-386, 2017
- Silbermann M, Arnaout M, Daher M, et al: Palliative cancer care in Middle Eastern countries: Accomplishments and challenges. *Ann Oncol* 23:15-28, 2012 (Suppl 3)
- Noun P, Djambas-Khayat C: Current status of pediatric hematology/oncology and palliative care in Lebanon: A physician's perspective. *J Pediatr Hematol Oncol* 34:S26-S27, 2012 (Suppl 1)
- Mutafoglu K, Ince D, Kutluk T: Availability of palliative care services for children with cancer in Turkey. *Asia Pac J Clin Oncol* 10:71, 2014 (suppl 10)
- Mutafoglu K, Ince D, Kutluk T: The current status of follow-up services for childhood cancer survivors in Turkish pediatric oncology centers. *Pediatr Blood Cancer* 61:S291, 2014 (suppl 2)
- Shamieh O, Hui D: A comprehensive palliative care program at a tertiary cancer center in Jordan. *Am J Hosp Palliat Care* 32:238-242, 2015
- Kebudi R; Turkish Pediatric Oncology Group: Pediatric oncology in Turkey. *J Pediatr Hematol Oncol* 34:S12-S14, 2012 (suppl 1)
- Saab R, Jeha S, Khalifeh H, et al: Displaced children with cancer in Lebanon: A sustained response to an unprecedented crisis. *Cancer* 124:1464-1472, 2018
- Ekmekci PE: Syrian refugees, health and migration legislation in Turkey. *J Immigr Minor Health* 19:1434-1441, 2017
- Spiegel P, Khalifa A, Mateen FJ: Cancer in refugees in Jordan and Syria between 2009 and 2012: Challenges and the way forward in humanitarian emergencies. *Lancet Oncol* 15:e290-e297, 2014

31. World Health Organization: WHO Model List of Essential Medicines for Children (April 2015). Geneva, Switzerland, World Health Organization, 2015
32. Cherny NI, Sullivan R, Torode J, et al: ESMO International Consortium Study on the availability, out-of-pocket costs and accessibility of antineoplastic medicines in countries outside of Europe. *Ann Oncol* 28:2633-2647, 2017
33. World Health Organization, Regional Office for the Eastern Mediterranean: WHO: Impact of fuel and drug shortages on patient care. OCHA Humanitarian Monitor. 2012. http://www.emro.who.int/images/stories/palestine/documents/pdf/6_Drug_Shortages_WBG_April_2012.pdf?ua=1
34. World Health Organization. Initial Health Assessment Report Gaza Strip. https://www.who.int/hac/crises/international/wbgs/WHO_Initial_Health_Assessment_Report_Gaza_Strip_-_December_2012.pdf
35. World Health Organization: Situation Report: Occupied Palestinian territory, Gaza 7-13 August, 2018. http://www.emro.who.int/images/stories/palestine/documents/WHO-Health-Cluster-SitRep-7-13_Aug.pdf
36. Salmasi S, Lee KS, Ming LC, et al: Pricing appraisal of anti-cancer drugs in the South East Asian, Western Pacific and East Mediterranean Region. *BMC Cancer* 17:903, 2017
37. Elias F, Bou-Orm IR, Adib SM, et al: Cost of oncology drugs in the Middle-Eastern country of Lebanon: An update (2014-2016). *J Glob Oncol* 4:1-7, 2018
38. Prices of more than 1,000 medicines, pharmaceutical products reduced. The Jordan Times, June 13, 2019. <http://www.jordantimes.com/news/local/prices-more-1000-medicines-pharmaceutical-products-reduced>
39. Yap ML, Zubizarreta E, Bray F, et al: Global access to radiotherapy services: Have we made progress during the past decade? *J Glob Oncol* 2:207-215, 2016
40. Atun R, Jaffray DA, Barton MB, et al: Expanding global access to radiotherapy. *Lancet Oncol* 16:1153-1186, 2015
41. Palestinian Health Capacity Project: Technical Brief 1 Rapid Assessment of Health Services Capacity in the West Bank. 2014. <https://www.intrahealth.org/sites/ihweb/files/files/media/rapid-assessment-of-health-services-capacity-in-the-west-bank/West%20Bank%20technical%20brief.pdf>
42. Bayram I, Erbey F, Komur M, et al: Treatment results of non-Hodgkin's lymphoma cases in cukurova region of turkey. *Erciyes Tip Derg* 33:23-28, 2011 http://www.erciyestipdergisi.org/pdf/pdf_EMJ_461.pdf
43. Kocak U, Gursel T, Kaya Z, et al: ALL-BFM 95 treatment in Turkish children with acute lymphoblastic leukemia—experience of a single center. *Pediatr Hematol Oncol* 29:130-140, 2012
44. Ali BAA, Abboud MR, Saab RH: Clinical prognostic factors in pediatric osteosarcoma: A single institution study. *J Clin Oncol* 33, 2015 (suppl 1) http://meeting.ascopubs.org/cgi/content/abstract/33/15_suppl/e21011?sid=a1f9e3a2-0a0d-494c-896f-69f5cc91b53c
45. Zulfikar B, Cakir F, Koc B: Excellent overall survival (100%) in Turkish children with standard risk acute lymphoblastic leukemia. *Pediatr Blood Cancer* 62:S92, 2015 (suppl 2)
46. Koc A, Aycecek A, Ozdemir ZC, et al: Outcome of modified St Jude total therapy 13A for childhood acute lymphoblastic leukemia in the southeast region of Turkey. *J Pediatr Hematol Oncol* 35:36-41, 2013
47. Muwakkit SA, Al-Aridi C, Samra A, et al: Implementation of an aggressive risk stratified treatment protocol for children and adolescents with acute lymphoblastic leukemia in a developing country. *Blood* 118:876, 2011
48. Rabeh W, Akel S, Muwakkit S, et al: Wilms tumor treatment and outcome at a multidisciplinary pediatric cancer center in Lebanon. *Pediatr Blood Cancer* 61:S384, 2014 (suppl 2)
49. Akyüz C, Yalçın B, Yıldız I, et al: Treatment of Wilms tumor: A report from the Turkish Pediatric Oncology Group (TPOG). *Pediatr Hematol Oncol* 27:161-178, 2010
50. Cecen E, Varan A, Sevinir B, et al: Treatment outcome of children with neuroblastoma under eighteen months of age treated according to the Turkish Pediatric Oncology Group Neuroblastoma 2009 (TPOG-NBL-2009) protocol. *Pediatr Blood Cancer* 60:110, 2013 (suppl)
51. Kutluk T, Yesilipek A: Pediatric cancer registry in Turkey 2009-2018 (TPOG & TPHD). *J Clin Oncol* 37, 2019 (15 suppl)
52. Kutluk M, Yesilipek A: Turkish national pediatric cancer registry 2002-2008 (Turkish Pediatric Oncology Group and Turkish Pediatric Hematology Society). *J Clin Oncol* 31, 2013 (15 suppl) http://meeting.ascopubs.org/cgi/content/abstract/31/15_suppl/10067?sid=86f76ae2-7226-4025-9d9b-12396251b2fc
53. Nimri O: Surveillance for Jordan cancer burden: Jordan cancer registry data 2010-2014. *J Glob Oncol* 4:241s, 2018 (suppl 2)
54. Bailony MR, Hararah MK, Salhab AR, et al: Cancer registration and healthcare access in West Bank, Palestine: A GIS analysis of childhood cancer, 1998-2007. *Int J Cancer* 129:1180-1189, 2011
55. Cecen E, Gunes D, Mutafoglu K, et al: The time to diagnosis in childhood lymphomas and other solid tumors. *Pediatr Blood Cancer* 57:392-397, 2011
56. Kutluk T: An economical analysis for the care of pediatric cancer patients. In: 50th Congress of The International Society of Paediatric Oncology SIOP, Kyoto, Japan, 2018
57. Elshahoubi A, Alnassan A, Sultan I: Safety and cost-effectiveness of outpatient administration of high-dose chemotherapy in children with Ewing sarcoma. *J Pediatr Hematol Oncol* 41:e152-e154, 2019
58. Al Rabayah AA, Jaddouh S, Amireh A: Cost minimization analysis of peg-l-asparaginase versus E. coli l-asparaginase in pediatric acute lymphoblastic leukemia (ALL) patients: A Jordanian perspective. *Value Heal* 19:A721-722, 2016
59. Meral Gunes A, Sezgin Evim M, Baytan B, et al: The treatment outcome of children with acute lymphoblastic leukemia: 20 Years experience from a single center in Turkey. *HemaSphere* 2:754-755, 2018 (suppl 2)
60. Akyüz C, Sari N, Yalçın B, et al: Long-term survival results of pediatric rhabdomyosarcoma patients: A single-center experience from Turkey. *Pediatr Hematol Oncol* 29:38-49, 2012
61. Sari N, Toğral G, Cetindağ MF, et al: Treatment results of the Ewing sarcoma of bone and prognostic factors. *Pediatr Blood Cancer* 54:19-24, 2010
62. Sultan I, Rihani R, Madanat F, et al: Survival gap for children with cancer in a middle-income country: lessons from King Hussein Cancer Center in Jordan. *Pediatr Blood Cancer* 61:S190-S191, 2014 (suppl 2)
63. Halalshah H, Abuirmeileh N, Rihani R, et al: Outcome of childhood acute lymphoblastic leukemia in Jordan. *Pediatr Blood Cancer* 57:385-391, 2011
64. Amayiri N, Jamal K, Nimri O: Epidemiology of pediatric primary CNS tumors in Jordan, 2001-2010. *Neuro-oncol* 18:iii41.2-iii41, 2016 (suppl 3)
65. Abou Ali B, Nader R, Tamim H, et al: Outcome of Ewing sarcoma in a multidisciplinary setting in Lebanon. *Pediatr Blood Cancer* 61:1472-1475, 2014
66. Gülses S, Yıldırım ZK, Büyükcavci M: Does the quality of life of children with cancer and their parents differ from that of patients with other diseases? *Cocuk Sagligi ve Hast Derg* 57:16-23, 2014
67. Arslan FT, Basbakkal Z, Kantar M: Quality of life and chemotherapy-related symptoms of Turkish cancer children undergoing chemotherapy. *Asian Pac J Cancer Prev* 14:1761-1768, 2013
68. Abu-Saad Huijjer H, Sagherian K, Tamim H: Quality of life and symptom prevalence in children with cancer in Lebanon: The perspective of parents. *Ann Palliat Med* 2:59-70, 2013
69. Brinksma A, Sanderman R, Roodbol PF, et al: Malnutrition is associated with worse health-related quality of life in children with cancer. *Support Care Cancer* 23:3043-3052, 2015 (suppl 1)

70. Yilmaz M, Sari HY, Kantar M, et al: Assessment of school-related problems of childhood cancer patients: A study from west of Turkey. *Pediatr Blood Cancer* 59:1009, 2012
71. Al Qadire M, Al-Sheikh H, Suliman M, et al: Predictors of anxiety and depression among parents of children with cancer in Jordan. *Psychooncology* 27:1344-1346, 2018
72. Ozbaran B, Erermis S, Kucukkose M, et al: Quality of life of children and adolescents in remission period of lymphoma and leukemia. *Psychooncology* 20:166, 2011 (suppl 1)
73. Farah R, Kouzy R, Kiwan P, et al: Long-term follow-up of childhood cancer survivors in Lebanon. *Pediatr Blood Cancer* 61:S305, 2014 (suppl 2)
74. Ergin D, Eser E, Kantar M, et al: Psychometric properties of the oncology module of the KINDL scale: First results. *J Pediatr Oncol Nurs* 32:83-95, 2015
75. Can G, Akin S, Aydinler A, et al: A psychometric validation study of the Quality of Life and FAMCARE scales in Turkish cancer family caregivers. *Qual Life Res* 20:1319-1329, 2011
76. Yavuz B, Bal Yilmaz H, Karaman N: A study of reliability and validity for the Turkish version of Children's International Mucositis Evaluation Scale for children with cancer. *Turk Onkol Derg.* 26:157-162, 2011
77. Özalp Gerçeker G, Bilsin E, Binay Ş, et al: Cultural adaptation of the Adolescent Pediatric Pain Tool in Turkish children with cancer. *Eur J Oncol Nurs* 34:28-34, 2018
78. Al-Gamal E, Long T: Psychometric properties of the Arabic version of the PedsQL Family Impact Scale. *J Res Nurs* 21:599-608, 2016
79. Sultan I, Al-Nassan A, Mansour A, et al: The cost of childhood cancer treatment in Jordan. *Pediatr Blood Cancer* 64:S431-S432, 2017
80. Bektas H: Quality of life of family caregivers in hematologic cancer. *Support Care Cancer* 21:S92, 2013 (suppl 1)
81. Al Qadire M, Aloush S, Alkhalaileh M, et al: Burden among parents of children with cancer in Jordan: Prevalence and predictors. *Cancer Nurs* [epub ahead of print on July 3, 2019]
82. Lakkis NA, Khoury JM, Mahmassani DM, et al: Psychological distress and coping strategies in parents of children with cancer in Lebanon. *Psychooncology* 25:428-434, 2016
83. Al-Gharib RM, Abu-Saad Huijer H, Darwish H: Quality of care and relationships as reported by children with cancer and their parents. *Ann Palliat Med* 4:22-31, 2015
84. Albarqouni L, Elessi K, Abu-Rmeileh NME: A comparison between health research output and burden of disease in Arab countries: Evidence from Palestine. *Health Res Policy Syst* 16:25, 2018
85. Phillimore P, Sibai AM, Rizk A, et al: Context-led capacity building in time of crisis: Fostering non-communicable diseases (NCD) research skills in the Mediterranean Middle East and North Africa. *Glob Health Action* 12:1569838, 2019
86. World Health Organization: Global Initiative for Childhood Cancer. 2018. <https://www.who.int/cancer/childhood-cancer/en/>
87. World Health Organization: Cancer prevention and control in the context of an integrated approach http://apps.who.int/ebwha/pdf_files/WHA70/A70_R12-en.pdf.
88. Neal C, Rusangwa C, Borg R, et al: Cost of providing quality cancer care at the Butaro Cancer Center of Excellence in Rwanda. *J Glob Oncol* 4:1-7, 2018
89. Greenberg ML, Barr RD, DiMonte B, et al: Childhood cancer registries in Ontario, Canada: Lessons learned from a comparison of two registries. *Int J Cancer* 105:88-91, 2003
90. Kroll ME, Murphy MF, Carpenter LM, et al: Childhood cancer registration in Britain: Capture-recapture estimates of completeness of ascertainment. *Br J Cancer* 104:1227-1233, 2011
91. Saxton AT, Bhattacharya M, Masalu N, et al: Cost-effectiveness of pediatric cancer treatment in Tanzania: An economic analysis. *J Glob Oncol* 3:33s, 2017 (2 suppl)
92. Sanchez-Zubieta F, Friedrich P, Galvez-Galvez B, et al: The cost and cost-effectiveness of a pediatric cancer unit (PCU) in the context of universal health coverage (UHC): A report from the Childhood Cancer 2030 Network. *J Clin Oncol.* 36:e18891, 2018 (15_suppl)
93. Fuentes-Alabi S, Bhakta N, Vasquez RF, et al: The cost and cost-effectiveness of childhood cancer treatment in El Salvador, Central America: A report from the Childhood Cancer 2030 Network. *Cancer* 124:391-397, 2018
94. Pramesh CS, Badwe RA, Sinha RK: The national cancer grid of India. *Indian J Med Paediatr Oncol* 35:226-227, 2014
95. Kulháňová I, Bray F, Fadhil I, et al: Profile of cancer in the Eastern Mediterranean region: The need for action. *Cancer Epidemiol* 47:125-132, 2017
96. GBD 2015 Eastern Mediterranean Region Cancer Collaborators: Burden of cancer in the Eastern Mediterranean Region, 2005–2015: Findings from the Global Burden of Disease 2015 Study. *Int J Public Health* 63:151-164, 2018
97. Reference deleted
98. World Health Organization: Regional Office for the Eastern Mediterranean Health: Strengthening health financing systems in the Eastern Mediterranean Region towards universal health coverage: Health financing atlas 2018. World Health Organization, Regional Office for the Eastern Mediterranean. 2019. <https://apps.who.int/iris/handle/10665/311328>
99. World Health Organization: Global Health Expenditure Database for Turkey. <https://apps.who.int/nha/database>



APPENDIX

TABLE A1. Literature Search Strategies

Database	Search Terms	No. of Hits
OvidSP		
1	(cancer* or carcinoma* or oncolog* or tumor* or tumor* or lymphoma* or sarcoma* or blastoma* or neoplas* or leuk?emia* or lymphoma* or blastoma* or glioblastoma* or medu?loblastoma* or nephroblastoma* or hodgkin* or rhabdomyosarcoma* or retinoblastoma* or neuroblastoma* or osteosarcoma* or h?epatoblastoma*).ti,ab	8,239,271
2	(child* or infant* or newborn* or youth* or teenager* or adolescen* or p?ediatric* or girl* or boy*).ti,ab	6,245,188
3	(turkey or turkish or jordan* or leban* or palestin* or gaza or "West Bank" or syria*).ti,ab	217,525
4	1 and 2 and 3	2,479
5	Remove duplicates from 4	1,657
6	Limit 5 to 2010 through current	1,050
Scopus		
1	TITLE-ABS-KEY(cancer* or carcinoma* or oncolog* or tumor* or tumor* or lymphoma* or sarcoma* or blastoma* or neoplas* or leuk?emia* or lymphoma* or blastoma* or glioblastoma* or medu?loblastoma* or nephroblastoma* or hodgkin* or rhabdomyosarcoma* or retinoblastoma* or neuroblastoma* or osteosarcoma* or h?epatoblastoma*)	5,018,685
2	TITLE-ABS-KEY (child* OR infant* OR newborn* OR youth* OR teenager* OR adolescen* OR p?ediatric* OR girl* OR boy*)	5,074,291
3	TITLE-ABS-KEY (turkey OR turkish OR jordan* OR leban* OR palestin* OR gaza OR "West Bank" OR syria*)	281,723
4	1 and 2 and 3	2,928
5	Limit 4 to 2010 through current	1,724
Web of Science		
1	TS=(cancer* or carcinoma* or oncolog* or tumor* or tumor* or lymphoma* or sarcoma* or blastoma* or neoplas* or leuk?emia* or lymphoma* or blastoma* or glioblastoma* or medu?loblastoma* or nephroblastoma* or hodgkin* or rhabdomyosarcoma* or retinoblastoma* or neuroblastoma* or osteosarcoma* or h?epatoblastoma*)	3,795,348
2	TS=(child* OR infant* OR newborn* OR youth* OR teenager* OR adolescen* OR p?ediatric* OR girl* OR boy*)	2,398,178
3	TS=(turkey OR turkish OR jordan* OR leban* OR palestin* OR gaza OR "West Bank" OR syria*)	225,293
4	1 and 2 and 3	913
5	Limit 4 to 2010 through current	588
EBSCO: Econlit with full text, CINAHL		
1	TX (cancer* or carcinoma* or oncolog* or tumor* or tumor* or lymphoma* or sarcoma* or blastoma* or neoplas* or leukemia* or leukemia or lymphoma* or blastoma* or glioblastoma* or meduloblastoma* or medulloblastoma or nephroblastoma* or hodgkin* or rhabdomyosarcoma* or retinoblastoma* or neuroblastoma* or osteosarcoma* or hepatoblastoma* or haepatoblastoma*)	734,199
2	TX (child* OR infant* OR newborn* OR youth* OR teenager* OR adolescen* OR p?ediatric* OR girl* OR boy*)	1,315,446
3	TX (turkey OR turkish OR jordan* OR leban* OR palestin* OR gaza OR "West Bank" OR syria*)	146,872
4	1 and 2 and 3	4,015
5	Limit 4 to 2010 through current	2,993

(Continued on following page)

TABLE A1. Literature Search Strategies (Continued)

Database	Search Terms	No. of Hits
WHO Global Index Medicus (IMEMR)		
1	Tw: (cancer* or carcinoma* or oncolog* or tumor* or tumor* or lymphoma* or sarcoma* or blastoma* or neoplas* or leukemia* or leukemia or lymphoma* or blastoma* or glioblastoma* or meduloblastoma* or medulloblastoma or nephroblastoma* or hodgkin* or rhabdomyosarcoma* or retinoblastoma* or neuroblastoma* or osteosarcoma* or hepatoblastoma* or haepatoblastoma*)	23,269
2	Tw: (child* OR infant* OR newborn* OR youth* OR teenager* OR adolescen* OR p?ediatric* OR girl* OR boy*)	32,774
3	Tw: (turkey OR turkish OR jordan* OR leban* OR palestin* OR gaza OR "West Bank" OR syria*)	3,849
4	1 and 2 and 3	59
Center for Reviews and Dissemination: NHSEED and HTA		
1	(cancer or carcinoma or oncology or neoplasm or tumor or tumor or lymphoma or sarcoma or blastoma or glioma) AND (turkey or turkish or jordan or jordanian or lebanon or lebanese or syria or syrian or palestine or palestinian or gaza or west bank) IN NHSEED, HTA	12

NOTE. OvidSP: Embase Classic + Embase, 1947 to July 17, 2019; Global Health: 1973 to week 27, 2019; HMIC: 1979 to May 2019, Ovid MEDLINE(R) ALL 1946 to July 17, 2019; PsycINFO 1806 to week 2, July 2019.

Abbreviations: ABS, Abstract; CINAHL, Cumulative Index of Nursing and Allied Health Literature; HTA, Health Technology Assessment; HMIC, Health Management Information Consortium; NHSEED, National Health Service Economic Evaluation Database; ti, title; ts, topic; tw, text word; tx, text word.