QATAR UNIVERSITY

COLLEGE OF ENGINEERING

IMPROVEMENT OF THE TIME TO DIAGNOSIS FOR ADULT LYMPHOMA

PATIENTS IN THE STATE OF QATAR:

A RETROSPECTIVE COHORT STUDY-BASED APPROACH

BY

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ABSTRACT

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Title: Improvement of The Time to Diagnosis for Adult Lymphoma Patients in The State of Qatar:

A Retrospective Cohort Study-Based Approach

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Prior to diagnosis, patients with Lymphoma might not recognize their symptoms, while others would assume that there is a simple explanation, therefore, they do not need a medical consultation. On the other hand, some patients would experience multiple primary care visits, resulting in referral and diagnosis delay, consequently, they often present as emergencies. This research will be carried based on a retrospective cohort study, using adult Lymphoma patients data from the National Center for Cancer Care and Research (NCCCR) database in Qatar. Using tools and techniques from data analytics, statistics and operations management, the data will be analyzed in order to achieve the main goals including; assessing the stage at diagnosis levels, benchmarking them with other countries, identifying factors associated with diagnosis delay, investigating the effect of stage at diagnosis on patients' survival, illustrating patients' current pathways to NCCCR, proposing improvements to shorten Lymphoma diagnostic pathway and assessing their effectiveness.

DEDICATION

This thesis is dedicated to the memory of my father, Mamdouh Abdelsalam, who has always believed in me, his guidance has made this journey possible. The dedication is extended to my mother, Aida Anwar, for her love and endless support, my husband, Sherif Moustafa, for his continuous encouragement during the challenges of graduate studies and life, as well to my brothers and sisters for never leaving my side.

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Chapter 1: Introduction

Cancer is a disease which can occur anywhere in the human body, it evolves when the body's normal control mechanism stops working, meaning that instead of dying, the old cells grow out of control, forming new abnormal cells, therefore, early cancer diagnosis is crucial for effective treatment and saving patients' lives. In the cancer diagnostic pathway, there are two vital time periods; the time between the first symptoms onset and first primary care consultation, the patient interval, as well, the time between consultation of a general practitioner (GP) and referral, the primary care interval.

1.1. Overview

Cancer may have begun to spread and became harder to be treated by the time symptoms are visible, that is why lack of awareness of the symptoms and untrained primary care GP can lead to referral delay. Moreover, the inability to distinguish cancer due common symptoms with other diseases can lead to excess referrals to secondary care, subsequently increasing the work load on waiting list and reducing patients' chance of having early consultation and diagnosis. This indicates that the duration of the patient interval and the primary care interval of the cancer diagnostic pathway could be extremely influenced by the nature of symptoms presentation.

Primary care is the phase where cancer suspicion, and risk factors assessment usually take place, including collection of family history, obesity and patients' unhealthy habits like smoking. It is seldom that a day passes in the primary care without raising cancer as a possible diagnosis. The symptoms base behind selection of patients for

referral continue to grow. Sometimes, the cause of symptoms is indefinite, that is when GPs need to trust their medical instinct. Most patients with easy-to-suspect cancer types such as Breast Cancer and Melanoma, are receiving good service from primary care. However, further exploration is needed to identify why patients with hard-to-suspect cancer types as Lymphoma, are experiencing diagnosis delay.

Further understanding of the factors impacting time to cancer diagnosis for patients within Qatar and investigating means of facilitation should be considered. According to The Ministry of Public Health, a total of 1,466 new cancer cases were diagnosed in 2015, including 1,417 malignant cases, out of which only 49 cases were diagnosed in early stage, that is about 3.46%. In addition, cancer deaths among Qataris for the same year accounted for 30% of all deaths related to cancer, having Breast Cancer as the most common cause with 19%, followed by Lung Cancer with 16.46% and Colorectal Cancer with 12.66%. Being a rapidly developing nation, along with the increase of the lifetime cancer risks, it is a call for an effective solution to tackle cancer and increase chances of early detection.

The significance of this research work is to understand the sources, extent, and root causes of Lymphoma diagnosis delays. In turn, this will help identifying areas for improvements to reduce diagnostic pathway intervals and will bring significant benefits to the treatment outcomes by increasing cancer survival rates, as well as minimizing patients suffer from having long treatment periods. Early diagnosis is also considered to be cost effective because diagnosing patients with advanced stage of cancer will require the usage of expensive novel drug therapies.

1.2. Aims and Objectives

Patients with Lymphoma often experience multiple primary care consultations, resulting in referral and diagnosis delay, therefore, they are more likely to present as emergencies. The aim of this research is to study adult Lymphoma cases, aged more than 14 years old, who are registered at The National Center for Cancer Care & Research (NCCCR) in Qatar, in order to assess the stage at diagnosis levels and identify barriers causing late diagnosis. The objective of this research can be identified as follow:

1. Assess stage at diagnosis of Lymphoma patients at the NCCCR.

2. Benchmark stage at diagnosis levels of Lymphoma patient in Qatar with other countries.

3. Identify factors causing Lymphoma diagnosis delay.

4. Investigate the effect of stage at diagnosis on patients survival.

5. Illustrate current pathways of Lymphoma patients.

6. Propose improvements to shorten Lymphoma diagnostic pathway.

7. Assess the effectiveness of the proposed improvements.

1.3. Project Scope

This research focuses on studying Lymphoma patients at NCCCR to promote improvements which will help in early detection and increase the chance of successful treatment. One of the main concerns of doctors at NCCCR, is that by the time of diagnosis, most patients have already reached advanced stage such as; stage III or stage IV of Lymphoma. Thus, they require the usage of high cost medications, minimizing the chance of treatment response and increasing patients suffer. By setting solutions for faster referral and diagnosis, Lymphoma treatment strategy in Qatar will be improved.

1.4. Research Plan

This research aims to introduce a solution to reduce Lymphoma fatalities in Qatar by enhancing the chance of early detection. This can be achieved through performing a retrospective analysis of patients data with the help of SPSS statistical software. The data under study represents a sample of Lymphoma patients, which is claimed from the NCCCR database and is covering the period of 2012 - 2017. The research is divided into three main phases:

<u>Phase 1: Literature Review (Chapter 2)</u>

Explore healthcare systems of well-developed countries such as Denmark, Canada, Sweden, and United Kingdom, which has identified cancer diagnostic pathway and were able to improve time to diagnosis of several cancer types. As well, to perform a gap analysis between their old and new state of performance to highlight major initiatives and draw conclusions.

Outcomes:

1.1. To analyze cancer diagnostic pathway of some developed countries.

1.2. To investigate diagnosis delay related factors.

1.3. To list applied initiatives for shortening cancer diagnostic pathway and their effectiveness.

<u>Phase 2: NCCCR Data Analysis and Patients Pathway Analysis (Chapter 3)</u>

Patients' willingness to require early contact to medical care is debatable, as some might not recognize their symptoms, while others would assume that there is a simple explanation and that they do not require medical consultation. Therefore, this study of the

claimed NCCCR data will identify common barriers causing patients' presentation delay and diagnostic delay.

In addition, understanding all possible pathways of Lymphoma patients to the NCCCR and analyzing them will identify the accessibility of NCCCR and barriers at the healthcare system leading to diagnostic delay. Such barriers are when primary care is assigned a gatekeeper role to limit the number of referrals to secondary care, or when the GP considers cancer so unlikely as not to require further examination. Consequently, a patient could experience multiple GP consultation and even present as an emergency.

Outcomes:

2.1. To assess stage at diagnosis levels of Lymphoma patients at the NCCCR.

2.2. To benchmark stages of Lymphoma for patients in Qatar with other countries.

2.3. To explore associations between patients-related factors and diagnostic delay.

2.4. To identify implications of stage at diagnosis on patients survival.

2.5. To illustrate the current pathways of Lymphoma patients.

Phase 3: Improvements for Shortening Lymphoma Diagnostic Pathway (Chapter 4)

Identifying areas for improving the effectiveness and efficiency of Lymphoma diagnosing process is crucial in order to be able to increase Lymphoma survival rates and to improve patients experience. This can only be achieved through shortening Lymphoma diagnostic pathway including; the patient interval and primary care interval.

Outcomes:

3.1. To propose improvements for shortening the patient interval and the primary care interval of the Lymphoma diagnostic pathway.

3.2. To assess the effectiveness of the proposed improvements.

Chapter 2: Literature Review

Cancer is a serious health problem associated with high mortality rates around the world and according to the World Health Organization, the number of cancer new cases is expected to rise by about 70% over the coming two decades. Therefore, we aim to assess cancer diagnostic pathway and its underlying intervals for Lymphoma patients in Qatar, in order to distinguish underlying cause of delays, including patient-, system-, and disease- related factors. This will help achieving early diagnosis, which in turn considered a key factor in improving treatment outcomes and identifying areas of potential improvements. Finally, Lymphoma types, symptoms and diagnosis process will be highlighted, as well, further investigation about developed countries' initiatives to reduce cancer diagnosis intervals will be carried out in order to identify their effectiveness and outcomes.

2.1. Cancer Diagnostic Pathway

The cancer diagnostic pathway can be divided into several intervals as shown in Figure 1. Its relevance differs between multiple healthcare systems, however, the Aarhus statement defined four important time intervals as a common international context (Weller et al., 2012). The patient interval (PI) is the time between noting the first symptoms and first consultation to primary care. The primary care interval (PCI) can be defined as the time between the first GP examining the patient and referral to secondary care for possible important pathology, including cancer. The secondary care interval (SCI) is the time from referral and first specialist visit to diagnosis. Finally, the treatment

interval (TI) is defined as the time from cancer diagnosis to start of treatment. There are some overlapping intervals like the diagnostic interval (DI) that include the time between the first presentation to primary care until receiving a diagnosis from secondary care, as well System interval (SI) that include the time between the first presentation to primary care to start of cancer treatment.
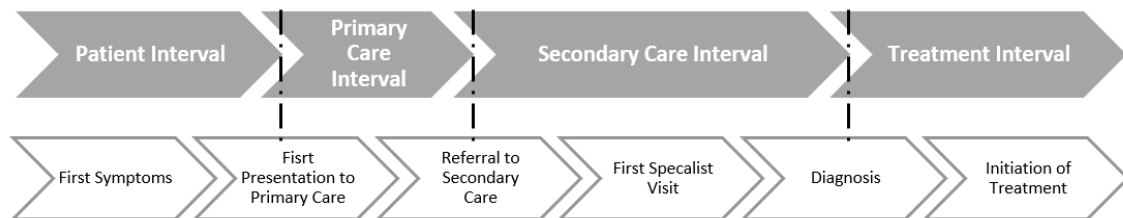
Figure 1. Cancer Diagnostic Pathway

Many countries have already of several of these intervals, but for other countries, such as Qatar, the duration of these intervals is unknown. The English National Awareness and Early Diagnosis Initiative (NAEDI) is considered one of the national initiatives with the aim of achieving early presentation of patients with symptoms, optimize clinical practice of GP and therefore early diagnosis. They consist of several work streams such as improving awareness by developing a validated measure of cancer symptoms and benchmarking current levels on a national basis.

Early stage cancer diagnosis will not only enhance treatment responsiveness and therefore survival rate but is also considered to be cost effective. This is because advanced stage of cancer requires the usage of expensive novel drug therapies (Field, Faragher, & Gibbs, 2011). Further to this, it is needed to focus efforts on shortening the cancer diagnostic pathway intervals and to strengthen cancer screening campaign to reduce economic burden.

Considering Breast Cancer being the highest incident cancer for United States female population, a published study covering two years has found that treating advanced stages is associated with a significant increase in cost. The average costs per patient in a year after diagnosis were "$60,637, $82,121, $129,387, and $134,682 for stage 0, I/II, III, and IV, respectively" while in two years were "$71,909, $97,066, $159,442, and $182,655 for stage 0, I/II, III, and IV, respectively" (Blumen, Fitch, & Polkus, 2016). The high cost is typically due expensive procedures such as Breast Cancer surgeries, chemotherapies, drugs radiation therapies and lap tests.

2.2. Patient Related Factors

Too little is known about patients' willingness to acquire early contact to primary care. Even though there is evidence that patients can identify which symptoms matter, most patients assume that there is a simple explanation for their symptom and that they do not need medical examination, others would not recognize their symptoms, as a result, many symptoms are not reported to primary care which could represent cancer. In case of patients experiencing more than single symptom, the combination of symptoms could sometimes encourage help-seeking and early presentation in primary care.

Some studies suggest that patients surpass to constantly visit the same doctor, this continuity in primary care has limited the debate to whether there are psychological and medical advantages from visiting the same doctor over time. Later it has been found that some patients prefer to not bother unnecessarily their own well-liked and trustworthy doctor, consequently could sometimes discourage case finding, which is referred to as "doctor induced patient delay" (Broom, 2003). The medical vigilance could also be

diminished due to the doctor's familiarity with the patient, therefore delaying cancer diagnosing and therefore reducing treatment outcomes.

Emotional and psychological barriers could strict some patients from seeking help because they are afraid of the results, embarrassed or not confident about expressing their symptoms to the doctor. Indeed, 27% of a sample of Danish population has proven to be worried what the doctor might find while 15% were worried that seeking help would waste their GP's time (Hvidberg, Wulff, Pedersen, & Vedsted, 2015). As a result, a patient might feel the need to delay medical consultant until they are confident they are qualified for one, this is out of a general perception that a GP's time and resources are scarce and precious (Cromme et al., 2016).

Some cancer types, such as Lung Cancer, patients might delay presenting at primary care due to the feeling of guilt, this is because that the main cause of cancer was that they have adapted unhealthy habits like smoking and by the time symptoms are reported, the cancer would have been spread, making treatment much harder. Also a Swedish study has found that women who believed that there is no cure for Breast Cancer even with early stage diagnosis, were less likely to participate in screening campaigns (Lagerlund, Hedin, Sparén, Thurfjell, & Lambe, 2000).

Gender, age, ethnicity and socioeconomic status are important factors for patients' presentation delay. A study applied in United Kingdom has found that awareness of cancer symptoms was less in those who were male, younger, and from ethnic minorities or lower socioeconomic status groups. Also, emotional barriers were more notable in lower socioeconomic status groups while practical barriers as being too busy or having more important things to worry about, were more notable in higher socioeconomic status

groups (Robb et al., 2009). Similar results have been found in Denmark as there were a strong association between having wrong beliefs about cancer with low educational and income levels. (Hvidberg et al., 2015).

Evidences indicates women aging more than 60 years with Breast Cancer symptoms are delaying first hospital visit, factors are related to concerns about financial consequences of seeking help, restrictions about consulting their GP, worries about the outcome of the diagnosis and cancer treatment process. In fact, up to third of women with Breast Cancer symptoms delay a minimum of three months before visiting a GP (C. C. Burgess et al., 2006). A United Kingdom general population survey found that the main reason that older women with Breast Cancer delay presentation is due their lack of knowledge about the symptoms and risk comparing to other age groups (Grunfeld, Ramirez, Hunter, & Richards, 2002).

In England and Wales, the leading cause of non-accidental death for teenagers and young adults aged 15 - 29 years is considered to be cancer with around 2,000 patients being diagnosed annually. The highest mortality rate was for Malignant tumors of the central nervous system followed by myeloid and monocytic leukemia, lymphoid leukemia, malignant bone tumors, and non-Hodgkin's Lymphoma (Geraci, Birch, Alston, Moran, & Eden, 2007).

By looking at teenagers and young adults age group diagnostic experience, it is often more complex and difficult. The main cause is that referral policy highly depending on presenting alarm symptoms, while most of the reported symptoms by teenagers are usually attributed to common conditions such as adolescent fatigue, sport injuries and stress (Fern et al., 2011).

2.3. System Related Factors

In a typical healthcare system, a primary care GP is usually assigned the role of gatekeeper to secondary care, meanwhile performing regular duties such as follow-ups, screening and minor illnesses treatment. The most remarkable argument against gatekeepers is that they constrain patient's freedom, and adversely affect patient–doctor trust since the later will have the right to approve on any referral to secondary care. On the other hand, in systems not embracing gatekeepers, patient can freely access secondary care to have further opinions if they felt a need for this.

Another serious cons of gatekeep systems is the long waiting time to have appropriate diagnosis from secondary care due to the long waiting lists. As well using gatekeepers as a cost containment tool, meaning that primary care shall provide the patients with the opportunity to repeatedly visit their GP and to exercise unjustifiable 'wait-and-see' behavior, thus limiting access to costly secondary care.

Over time, gatekeeper-based systems will affect the GPs responsiveness to patients' medical needs, and in some cases, they might not refer patients until symptoms become more visible. This is because GPs do not want to be judged badly by secondary care doctors as if they were referring unnecessarily. In fact, a study has found that healthcare systems with primary care gatekeeping is associated with 1-year lower survival rates than systems without a gatekeeper function (Vedsted & Olesen, 2011).

These findings have highlighted the cancer diagnosis delay resulting from having long duration of primary care interval. Consequently, the importance of having a strong primary care has started to be recognized worldwide, with a particular focus on the

potential role of the GP in the diagnostic process, that is to ensure referral of patients in need to the secondary care at the right time.

Given United Kingdom as examples, it has been noticed that it has a lower cancer prediction than most countries, even though its healthcare system is considered one of the high quality systems (Hamilton, 2010). In fact, it has been stated that 5,000 - 10,000 patients die each year from cancer due to diagnosis delay in United Kingdom (Richards, 2009), that is because of its strict gatekeeper-based healthcare system, which resulting to exclusive access to secondary care through referral from primary care.

Same as for Denmark, it has been observed that most cancer patients have experienced a considerable diagnostic delay dominated by system-related factors (Olesen, Hansen, & Vedsted, 2009), which is due long waiting list for initial diagnosis in the secondary care, consequently causing the GP to hesitate to refer additional patients. A time interval study made in Denmark has resulted in a median total delay of 98 days for the 10 most frequent cancers diagnosed among the study patients, out of which 55 days were related to system delay in secondary care (Hansen, Vedsted, Sokolowski, Søndergaard, & Olesen, 2011).

A GP's referral priority behavior could also affect time to diagnosis cancer. Examining referral priority for common cancer types in Scotland, it has been found that 11.7% of colorectal cancer patients were more likely to present as an emergency admission, 77.5% of Breast Cancer patient were referred urgently while 38.6% of Prostate Cancer patients referred to hospital routinely (Baughan, O'Neill, & Fletcher, 2009). The priority of referral could contribute considerably to delays as patients referred urgently would experience shorter time to see a specialist than patients referred routinely.

A strong primary care system can deliver better patient experience and sometimes the late referral for common cancer types occurs due to either the GP within primary care has lack of expertise of symptoms or that they consider them so unlikely as not to require examination or investigation. In case of Breast Cancer, older women were less likely than younger women to experience delays because of the GP's late referral for diagnosis (C. Burgess, Ramirez, Richards, & Love, 1998). While for cancers which present non-specific symptoms as multiple myeloma, patients would experience minimum of three consultations before having referral (Rubin et al., 2012).

2.4. Disease Related Factors

Understanding the nature and frequency of symptoms presentation for different cancer types is required before exploring how symptoms may impact diagnostic intervals. Depending on cancer type, around 10-25% of cancer patients show considerably long duration of diagnostic intervals (Helsper, van Erp, Peeters, & de Wit, 2017). In fact, the primary care interval for cancers with visible symptoms such as Breast Cancer are usually short, as patients mostly present with breast pain, breast lump and skin irritation or dimpling.

Symptoms are considered much common, for Ovarian Cancer and are generally reported to GPs, such as abdominal pain and distension, fatigue and urinary frequency. One study in Denmark has confirmed this findings after calculating the total delay for the 10 most frequent cancers diagnosed among study patients. The shortest total delay was noticed for Ovarian Cancer with median of 60 days, followed by Breast Cancer with median of 65 days (Hansen et al., 2011).

While for cancers with non-specific nature of symptoms such as Lung Cancer is considered relatively long. Patients usually present cough, dyspnea, loss of appetite, and chest pain, so it is often difficult to identify that cancer is the cause, even if the patient presents early. In United Kingdom, an average of 20% of Lung Cancer patients are eligible for surgical resection, only 17% actually undergo surgery, and around half of those survive for 5 years (Hamilton, 2010). The same situation is for Colorectal Cancer, where patients come to primary care usually with abdominal pain, rectal bleeding and bleeding accompanied by either diarrhea or constipation, that is why it is usually misdiagnosed. In advanced stages patients are subject to iron-deficiency anemia, consequently very high mortality risks.

This led us to divide cancer symptoms signature, which is defined as the frequency of symptoms reported to the GP and later diagnosed with cancer, into two types; narrow and broad (Koo, Hamilton, Walter, Rubin, & Lyratzopoulos, 2018). Narrow symptom signature is when most patients report particular symptoms with sufficiently strong association with a specific cancer type, as in the case of Breast Ovarian and Testicular Cancers. While, broad symptom signature is when patients report a larger range of symptoms as in the case of Lung- and Colorectal- Cancer.

Notably, a narrow symptom signature does not necessarily promise easier diagnosis for all patients. Given sarcoma as an example, the narrow nature of its symptoms; soft tissue lumps or bone pain, is associated with a suggestion to be low level of diagnostic difficulty, however, due rarity of sarcomas among the general population, alternative diagnoses are often provided (Smith, Johnson, Grimer, & Wilson, 2011).

Also, a broad symptom signature does not guarantee difficult diagnosis for all patients. If patient present certain alarm symptom, as rectal bleeding in the context of Colorectal Cancer, then it became a strongly predictive of cancer (Koo et al., 2018). Therefore, we can say that the symptom signature of a cancer is closely tied to its diagnostic difficulty.

In case of a combination of broad and nonspecific symptoms, the diagnosis becomes considerably difficult, as in case of Lymphoma. Patients usually report fatigue, weight loss and back pain, consequently, result to having multiple consultations in primary care before referral to secondary care. Patients with Brain Cancer report broad and nonspecific symptoms as well, thus, they are only diagnosed after an acute event such as having seizures (Hamilton & Kernick, 2007).

Cancer size and growth rate is considered vital factors for diagnosis. Given Prostate Cancer as an example, the treatment of small tumors does yield lives savings, but at a cost of possible complications such as incontinence, however, treatment of larger tumors, and of disease that has spread is much less debatable as those are more likely to reveal the symptoms (Walsh, 2002).

Also, there is a correlation between cancer site and the time taken for a patient to notice symptoms and consult a GP. A Scotland study has found that Head and Neck, Melanoma and Colorectal Cancers took the longest time before seeking help from a GP with a median of 30, 26 and 21 days respectively while Bladder, Leukemia, Cervical and Breast Cancers took the shortest time with a median of 2, 4, 6.5, 7 days (Baughan et al., 2009).

2.5. What is Lymphoma?

This type of cancer could begin in any part of the human immune system, including lymph nodes and vessels, spleen, bone marrow, thymus, digestive tract, adenoids and tonsils as shown in Figure 2. Traditionally Hematological Cancer is categorized into three main groups; Lymphoma, Myeloma and Leukemias, which in turn comprise more than 60 different subsystems, each, behave, spread, and respond to treatment differently. Patients present different pattern of symptoms resulting in multiple primary care consultations and diagnostic delay.

In case of Lymphoma, including Hodgkin and Non-Hodgkin Lymphoma, a single node or a group of lymph nodes in an area may swell or enlarge as they work to filter out the cancer cells. Some of the most commonly lymph nodes to swell are located in the neck, groin and underarms areas. Only one lymph nodes area could swell at a time, if it spreads through lymph vessels, more than one lymph nodes area is swollen. In advanced stages, it can invade nearby organs as well.
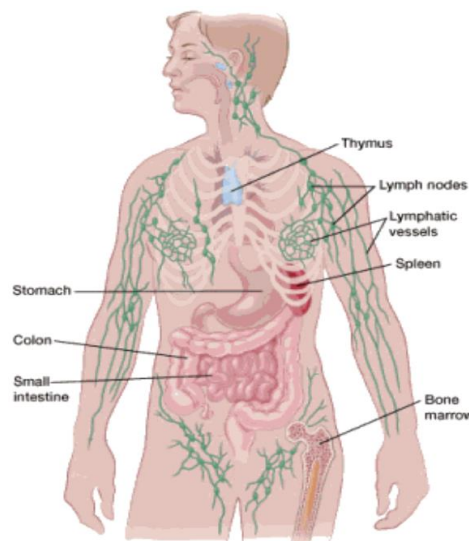
Figure 2: Major Sites of Lymphoid Tissue

Hodgkin Lymphoma (HL) commonly starts in B cells within lymph nodes located in chest, neck, or under arms. HL are two types; Classic Hodgkin Lymphoma (CHL) and Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL), but The CHL is the most common (American Cancer Society, 2018). While Non- Hodgkin Lymphoma (NHL) usually starts in white blood cells called lymphocytes within lymph nodes or other lymph tissue. NHL are two types; Non- Hodgkin Lymphoma B-Cells and Non- Hodgkin Lymphoma T-Cells, but the B-Cells is the most common (American Cancer Society, 2018).

For most cases, patients develop Lymphoma in their early twenties and late adulthood, however it could affect children and teenagers. Also, males are slightly more often to develop Lymphoma than females. As well, a history of first degree relatives could be an indicator of high risk to develop Lymphoma. Other high risk factors could be having a weakened immune system such as the case of organ transplant and taking immune system suppression medicines. Also, having certain infections such as Human Immunodeficiency Virus (HIV), Epstein-Barr virus (EBV) and Human herpes virus 8 (HHV-8). In addition to having radiation and certain chemicals exposure such as benzine (American Cancer Society, 2018).

Lumps found in the upper part of the body is a major sign that require medical investigation as Lymphoma could be the cause. Some patients experience what is called B symptoms which include; unexplained fever, night sweat, and weight loss. These symptoms are specific to Lymphoma and they often means that the patient is in a advanced stage. Other non-specific symptoms are itching skin, fatigue and loss of appetite. Additional symptoms may appear depending of the affected lymph nodes, for

example, if HL affected lymph nodes inside the chest, then the patient might experience chest pain, cough and trouble breathing (American Cancer Society, 2018).

In order to diagnose Lymphoma, a patient need to undergo some test such as; taking a biopsy of a lymph node or tissue, a Complete Blood Count (CBC) to identify the levels of different types of cells in the blood, a bone marrow aspiration and biopsy to tell if Lymphoma has reached the bone marrow, a chest x-ray or Computed Tomography (CT) scan to look for swollen lymph nodes in the body, a Magnetic Resonance Imaging (MRI) scan to tell if Lymphoma has reached the spinal cord or brain, finally, a Positron Emission Tomography (PET) scan to show where Lymphoma has been spread (American Cancer Society, 2018).

After diagnosing Lymphoma, the staging process is essential to sum up the extent of cancer spread. The staging system used is the Lugano Classification, which is based on the older Ann Arbor system. It has 4 stages, labeled I, II, III, and IV. For limited stage (I or II) Lymphomas that affect an organ outside the lymph system, the letter E is added to the stage, for example, stage IE or IIE (American Cancer Society, 2018).

- **Stage I:**

  - Lymphoma is found in only 1 lymph node area or lymphoid organ (I).

  - Lymphoma is found only in 1 area of a single organ outside the lymph system (IE).

- **Stage II:**

  - Lymphoma is found in 2 or more groups of lymph nodes on the same side of the diaphragm (II).

- Lymphoma extends locally from one lymph node area into a nearby organ (IIE).

  - **Stage III:**

    - Lymphoma is found in lymph node areas on both sides of the diaphragm.

    - Lymphoma is in lymph nodes above the diaphragm and in the spleen.

  - **Stage IV:**

    - Lymphoma has spread widely into at least one organ outside the lymph system, such as the liver, bone marrow, or lungs.

Both of stage I and II are considered early stages of Lymphoma because the cancer cells are located within one side only of the diaphragm, allowing for more effective cancer containment by treatment. On the other hand, advanced stages of Lymphoma are stage III and IV, since cancer cells have already spread to the other side of the diaphragm, which require harder treatment. Stage IV is the most advanced stage as cancer cells have moved into other tissues and organs beyond the lymph system. For the time being, screening is not widely recommended for HL as it showed that it doesn't lower the risk of dying from Lymphoma, however, early reporting of specific symptoms such as an enlargement or swelling of one or more lymph nodes could boost early diagnosis (American Cancer Society, 2018).

Promoting early diagnosis is particularly challenging yet is essential as Hematological Malignancies are common in economically developed regions of the world, being the fourth most frequently diagnosed cancer in both males and females (Howell et al., 2015), as well accounting for around one in ten of all new cancer

diagnoses (Howell et al., 2013). A study was carried out in United Kingdom, which examined the time taken for patients to consult a GP for several Hematological Malignancy subtypes to be more than 3 months, which have a high negative effect on patients medical situation (Forbes, Warburton, Richards, & Ramirez, 2014).

In United Kingdom, a survey about symptoms was distributed on patients with Acute Leukemia, Chronic Lymphocytic Leukemia, Chronic Myeloid Leukemia, Myeloma and Non-Hodgkin Lymphoma. It has been found that out of the 785 respondents, 654 (83.3%) reported at least one symptom, most commonly for non-Hodgkin Lymphoma (95%) followed by acute leukemia (91.6%), chronic myeloid leukemia (83.2%), myeloma (78.7%) and least commonly for chronic lymphocytic leukemia (67.9%), considering that the presence or absence of symptoms varied by diagnostic group (Howell et al., 2015).

Hematological Cancers signs are often subtle, the most common systematic symptom reported by patients was extreme fatigue or tiredness (50.8%), while for pain-, chest-, lump, and bleeding symptoms, they were bones pain (27.7%), shortness of breath (26.5%), lump in neck or armpit (21.3%) and unusual bruising or rash/red spots (14.7%) respectively (Howell et al., 2015), thus they considered a challenge for GP.

Delay in presentation can lead to advanced stage at diagnosis which in turn may contribute to poor cancer survival. Barriers that faced patients with Hematological Cancer varies, some argued the accessibility to appointments, while others did not seek medical help earlier because they did not realize the seriousness of their symptoms, others worried about wasting doctor's time or what doctor might find, and some patients mentioned that they were too busy to go to doctor.

2.6. Worldwide Initiatives to Shorten Cancer Diagnostic Pathway

Initiatives could be at community level such as screening and symptoms awareness, or at individual level such as education programs. All types of initiatives can achieve early cancer detection; however, its effectiveness differ among cancer types. Initiative could be also in form of increasing availability of the appropriate diagnostic tests, establishing service target, initiating programs as well introducing guidelines and diagnosis frame work to be followed by GPs, all which could boost early presentation and reduce cancer diagnostic pathway. A summary of worldwide initiatives to reduce cancer diagnostic pathway is stated in Table 1.

The first suggestion to overcome late diagnosis for Lung Cancer was screening. yet, it has little to offer. For example, applying conventional sputum cytology on patients with potential Lung Cancer will have very low sensitivity same as plain chest X-ray. On the other hand, organized mammography screening has higher incident to detect Breast Cancer at early stage.

In Sweden, after a follow-up period of 5 to 13 years, screening was able to reduce mortality rate by 29% for women aged 50-69 years and by 13% for women aged 40-49 years (Nystrom & Rutqvist, 1993). Another study on Colorectal Cancer covering two regions in England has suggested that the awareness campaign caused a 10% increase for one month in presentation rates to GPs (Whyte & Harnan, 2014). However, convincing people to participate in screening campaign is a little challenging. For example, in Denmark only 75-80% of women invited for Breast Cancer screening did participate in the campaign (Langagergaard et al., 2013).

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Therefore, efforts have been made to increase symptoms awareness, consequently, increasing the chance of earlier presentation. A campaign in United Kingdom has started to encourage patients with a cough to report it to their GP to request a chest X-ray. As a result, the percentage of Lung Cancer identified in stages I or II has increased from 11% to 19% (Hamilton, 2010).

Education programs for GP including lectures, training sessions and videos could improve knowledge of risk factors, diagnostic ability and reduce unnecessary referrals. However, traditional education programs having passive audience participants would have less positive effect than modern methods with active audience participants.

A study evaluating the impact of Skin Cancer education on twenty-three GPs' diagnostic skills randomized into two groups and each showed a different set of clinical slides had concluded a significant improvement in GPs' diagnostic ability from 63% and 55% to 76% and 62%, respectively after attending an education lecture supplemented by illustrated booklet (Bedlow et al., 2000).

Another study has evaluated the effect of educational intervention on 130 female employees of Zahedan University of Medical Sciences at improving breast cancer early diagnosis, which has confirmed a positive effect, including knowledge increase of breast cancer preventive behaviors among participants (Eskandari-Torbaghan, Kalan-Farmanfarma, Ansari-Moghaddam, & Zarei, 2014).

The variation in the number of medical consultations for different cancer types before referral reflects the lack of availability of or access to appropriate diagnostic tests, or both, nevertheless the lack of GP's knowledge and poor medical performance. Thus, improving observational skills, decision accuracy and including additional resources to improve access to diagnostic tests is a key component for a new diagnostic strategy.

Indeed, Lung Cancer diagnosis is considered easier than most other cancer types as the main test, a chest X-ray, is reasonably cheap, quite accurate and easily available. However, it would be even more efficient to have a policy to choose which patients shall have a chest X-ray such as all smokers over 50 years presenting to primary care with a cough or those who present with hemoptysis symptom. On the other hand, the main test for Colorectal Cancer is colonoscopy, which is considered uncomfortable and costlier, even though it has good performance.

Establishing a service target following a GP referral for the patient to be examined by a specialist is considered one of the potential initiatives to reduced diagnosis interval. For all cancer types, such service target has been set in United Kingdom in 2000, known as the 2-week-wait (2ww). This involves referral of patients within 24 hours by a GP if cancer is suspected and specialist consultation within 2 weeks (Mansell, Shapley, Jordan, & Jordan, 2011). Yet, no conclusions were made concerning the 2ww intervention in reducing diagnostic delay.

The Cancer Fast-track Program was one of Spain initiatives to reduce time to diagnosis and start of treatment for Breast, Colorectal and Lung Cancers. It was launched in 2005, and was able to detect 50% of new cancer cases in the period of 2006–2009 (Prades, Espinàs, Font, Argimon, & Borràs, 2011). All patients suspected with cancer

were included in this pathway and were set a 30 days period to receive a diagnosis, thus mad a considerable contribution in accelerating cancer diagnosis process.

Currently, as many as a quarter of people are still diagnosed with cancer after emergency presentation to secondary care (Elliss-brookes et al., 2012), thus a very effective solution to assist early diagnosis is to introduce some guidelines and diagnosis frame work to be followed by GPs in primary cares. For primary care with strict gatekeeper role, some countries have introduced what is called "urgent referral" to be used by GP to refer patients presenting suggestive cancer symptoms (Round, 2017), which has proven to reduce time to diagnosis for many cancer types.

United Kingdom as an example, have introduced in 2005 the National Institute for Health and Care Excellence (NICE) guidelines on urgent referral and a study made on 15 cancer types had showed that the overall mean diagnostic interval reduced by 5.4 days between 2001-2002 and 2007-2008 (Neal et al., 2014). However, the excessive usage of urgent referral could have counter effects on diagnosis time as it would cause bottlenecks in the system. Therefore, treatment outcome is highly dependent on cancer type and stage at diagnosis time.

The Danish government have also introduced Cancer Patient Pathways (CPPs) guidelines in 2008 with the attempt to reduce delays in diagnosing and treating cancer though standardizing time frames for diagnosis and treatment procedures. A survey made in 2010 in Denmark found that the median length of the diagnostic interval for the five most common cancer was shorter after the CPP implementation.

Despite that, only around 40% of patients have benefitted from CPP implementation as patients who were not referred to a CPP in 2010 still had long diagnostic intervals similar as before the implementation of CPPs (Jensen et al., 2015). This demonstrates the need to provide a more focused and faster diagnostic pathways for the large groups of patients who are not referred to a CPP in the early stage of their disease.

Most guidelines mainly focus on alarm symptoms accompanying a GP suspicion of cancer, but studies have proven that only 50% of patients diagnosed with cancer present alarm symptoms in initial phases. Thus, such guidelines could have negatively affected a large group of patients presenting non-specific symptoms.

As a result, Denmark has introduced NSSC-CPP in 2012 that consist of two steps, a GP initial assessment through undergoing investigation tests such as blood test, and this step is completed within eight days. Second step is a referral to a diagnostic unit at the hospital level which allow faster access to expertise in relevant specialties and diagnostic tests, and this step is completed within 22 days. In fact, a study made in 2017 has showed that 11% of patients referred to NSSC-CPP were diagnosed with cancer, out of which 18% were diagnosed with Breast Cancer, 15% with Hematopoietic and Lymphoid Tissue Cancer, and 12% with Malignant Melanoma (Moseholm & Lindhardt, 2017).

Some countries have applied lifestyle factors-oriented initiatives. Considering lifestyle factors, for Denmark, having a high number of smoking citizens, resulting to a relatively high cancer incidence. In fact, among many Western European countries, Denmark has poorer 5-year cancer survival rates (Berrino et al., 2009). As a result, their

initiatives were launched to encourage population to adopt healthier lifestyle through increase exercise, promote healthier diets and reduce smoking (Olesen et al., 2009).

On the other hand, Canada has offered GPs at primary care a free online accredited education course on early Lymphoma cancer detection, due to the lack of available education and resources for GPs at that time, to overcome the late referral and diagnosis issues. The course was released in June 2012 and its goal was to review the incidence of Lymphoma in Canada, describe its clinical indicators and discuss approaches for early recognition in clinical practice.

At the first three months after releasing the course, 64% of the 908 participants were GPs and results showed that there was a significant change in behavior from questions asked pre- and post-course. Also, out of the 454 participants who have completed the pre-course survey, 36.25% said they were likely to screen for Lymphoma in a patient with persistent lymphadenopathy, however, that number increased to 78% after completing the course (Lymphoma Canada, 2013).

Table 1: Summary of Initiatives to Reduce Cancer Diagnostic Pathway

Reference	Country	Cancer type	Nature of Symptoms	Initiatives	Effectiveness	Observations
(Hamilton & Kernick, 2007)	United Kingdom	Lung	Non-specific	Screening	Not Effective	Sensitivity of Tools are too low to detect cancer in early stages
(Nystrom & Rutqvist, 1993)	Sweden	Breast	Specific	Screening	Effective	After a follow-up period of 5 to 13 years, mortality rate was reduced by 29% for women aged 50-69 years and by 13% for women aged 40-49 years
(Whyte & Harnan, 2014)	England	Colorectal	Specific	Screening	Effective	The awareness campaign caused a 10% increase for one month in presentation rates to GPs
(Hamilton & Kernick, 2007)	United Kingdom	Lung	Non-specific	Symptoms Awareness	Effective	The percentage of cancers identified in stages I or II increased from 11% to 19%

(Bedlow et al., 2000)	United Kingdom	Skin	Specific	GP Education Programs	Effective	Significant improvement in GPs' diagnostic ability for two study group from 63% and 55% to 76% and 62%
(Eskandari-Torbaghan, Kalan-Farmanfarma, Ansari-Moghaddam, & Zarei, 2014).	Iran	Breast	Specific	Educational Intervention	Effective	Educational intervention on 130 female employees of Zahedan University of Medical Sciences has confirmed a positive effect, including knowledge increase of breast cancer preventive and early diagnosis behaviors
(Mansell, Shapley, Jordan, & Jordan, 2011)	United Kingdom	All Cancers	Specific/ non-specific	2ww service target	Not identified	No conclusions were made concerning the 2ww intervention in reducing diagnostic delay
(Prades, Espinàs, Font, Argimon, & Borràs, 2011)	Spain	Breast Colorectal Lung	Specific/ non-specific	Cancer Fast-track Program	Effective	The program has contributed to speeding up diagnostic assessment and treatment of patients

(Neal et al., 2014)	United Kingdom	Kidney Head and neck Bladder Colorectal Esophageal pancreatic	Specific/ non-specific	2005 NICE Referral Guidelines	Effective	Significant reduction in mean diagnostic interval from 2001-2002 to 2007-2008
(Jensen et al., 2015)	Denmark	All Cancers	Specific	CPPs Referral Guidelines	Effective	The median length of the diagnostic interval was shorter after the CPP implementation for patients with alarm symptoms
(Moseholm & Lindhardt, 2017)	Denmark	All Cancers	Non-specific	NSSC-CPP Referral Guidelines	Effective	11% of patients referred to NSSC-CPP were diagnosed with cancer
(Lymphoma Canada, 2013)	Canada	Lymphoma	Non-specific	Online Accredited Education Course	Effective	Significant change in questioning and screening behavior

Chapter 3: NCCCR Data Analysis and Patients Pathway Analysis

In order to assess the stage at diagnosis of adult Lymphoma patients in Qatar, the claimed data from NCCCR will be evaluated with respect to the time factor for diagnosing Lymphoma, then, the stage at diagnosis results will be benchmarked with other countries. Following to that, some common factors which may cause presentation and diagnostic delays of Lymphoma will be investigated including; patients' gender, age and nationality. Finally, the effect of stage at diagnosis on the patients in terms of the survivability rate will be assessed, in addition to investigating the current pathway of Lymphoma patients to reach NCCCR.

3.1. Research Limitation

Some clarifications must be made with regard to the data, the Multi-Disciplinary Team (MDT) meeting date was considered as the Lymphoma diagnosis date, even though, Lymphoma might has been already diagnosed before that date. Moreover, early stages are considered to be stage I and stage II, while advanced stages are considered to be stage III and stage IV as cancer cells would have spread to both side of the diaphragm. Also, for the stage at diagnosis benchmarking with other countries, different years period have been used due to lack of available information, yet, all periods are overlapping.

Finally, for the assessment of patient related factors, the collected data have included age, gender, nationality, MDT meeting date, last follow up date, life status and diagnosis stage, however, other essential data related to the patients' socioeconomic status, was not available for assessment. In addition, for the patient's nationality factor

assessment, the total number of people from each nationality which were living in Qatar at 2017 was assumed for the following eight nationalities; Cameroonian, Mauritanian, Somalian, Bahraini, Kuwaiti, Omani, Saudi and Yemeni, in order to normalize the number of cases, which is mainly because of the privacy of such information.

3.2. Data Collection

The study consisted a sample of 414 adult Lymphoma patients aged between 14 and 94 years old residing in Qatar, including 108 Hodgkin Lymphoma (HL) cases and 306 Non-Hodgkin Lymphoma (NHL) cases. All data was extracted from NCCCR Database covering the period of 2012-2017. The HL cases included 16% for Predominant Hodgkin Lymphoma and 84% for Classical Hodgkin Lymphoma as shown in Figure 3, while NHL cases included 12% for B-Cell Non-Hodgkin Lymphoma and 88% for T-Cell Non-Hodgkin Lymphoma as shown in Figure 4.
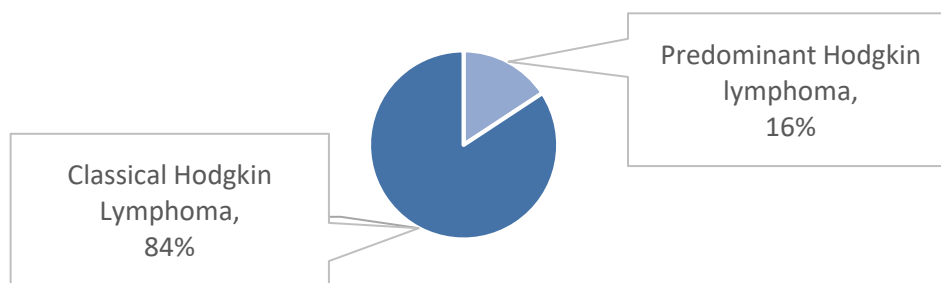
Figure 3: Major Subtypes of Hodgkin Lymphoma Cases at NCCCR
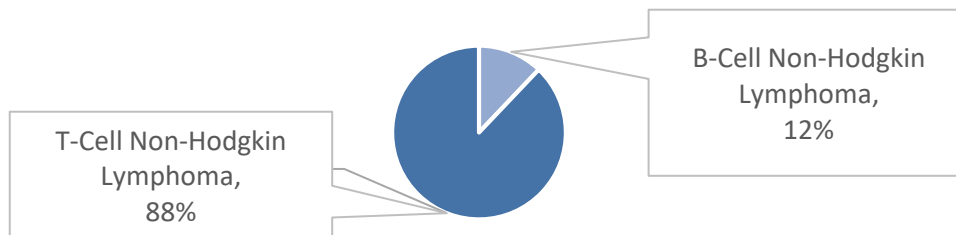
Figure 4: Major Subtypes of Non-Hodgkin Lymphoma Cases at NCCCR

3.3. Stage at Diagnosis Assessment of NCCCR Patients

Generally, there are 108 HL cases recorded in the NCCCR database over the period of 2012-2017 out of which a total of 56.48% were diagnosed at advanced stage, including 21.30% at stage III and 35.19% at stage IV as shown in Table 2. Over the same period, the percentage of advanced stage cases have been increasing annually as Figure 5 shows the increasing peaks, however, there is one trough at the year of 2015. Generally, there is a total of 28% increase in the number of advanced stage cases over the mentioned six years, being the highest at 2017 and 2016 with 68.00% and 65.38% respectively.

Table 2: NCCCR Hodgkin Lymphoma Cases 2012-2017

Year	Number of Patients	Stage I	Stage II	Stage III	Stage IV	Stage III (%)	Stage IV (%)	Advanced Stage (%)	Early Stage (%)
2012	10	3	3	0	4	0.00	40.00	40.00	60.00
2013	17	3	6	3	5	17.65	29.41	47.06	52.94
2014	17	3	5	3	6	17.65	35.29	52.94	47.06
2015	13	5	2	4	2	30.77	15.38	46.15	53.85
2016	26	3	6	8	9	30.77	34.62	65.38	34.62
2017	25	2	6	5	12	20.00	48.00	68.00	32.00
Total	108	19	28	23	38	21.30	35.19	56.48	43.52
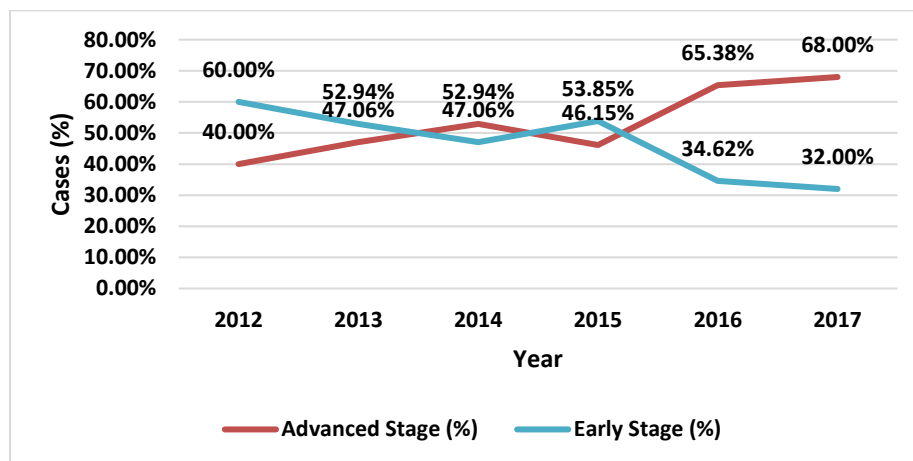
Figure 5: Stage at Diagnosis Trends of Hodgkin Lymphoma 2012-2017

By comparing the annual diagnosed cases at each year for each stage, there were a maximum of 5 cases diagnosed with stage I HL, a maximum of 6 cases diagnosed with stage II, a maximum of 8 cases diagnosed with stage III, while a maximum of 12 cases diagnosed with stage IV at least in one year within the mentioned period. The mean and standard deviation of the annual diagnosed cases with 95% confidence interval were the largest for stage IV with 6.33 and 3.615 respectively as shown in Table 3 which suggest a potential late diagnosis problem of HL at the NCCCR.

Table 3: Descriptive Statistics of 2012-2017 Hodgkin Lymphoma Cases

	Minimum	Maximum	Mean	Std. Deviation
Stage I	2	5	3.17	0.983
Stage II	2	6	4.67	1.751
Stage III	0	8	3.83	2.639
Stage IV	2	12	6.33	3.615

The same result could be concluded by comparing the mean and standard deviation of the total annual number of early and advanced stage cases. As shown in Table 4, the 10.17 mean and 5.565 standard deviation of advanced stage cases is higher than the 7.83 mean and 1.169 standard deviation of early stage cases.

Table 4: Descriptive Statistics of Annual Hodgkin Lymphoma Staging

	Total Early Stage	Total Advanced Stage
2012	6	4
2013	9	8
2014	8	9
2015	7	6
2016	9	17
2017	8	17
Total	47	61
Mean	7.83	10.17
Std. Deviation	1.169	5.565

On the other hand, the recorded number of NHL cases at the NCCCR database is significantly higher than HL cases because it is considered more common. In fact, over the period of 2012-2017 there were 306 cases out of which a total of 68.95% were diagnosed at advanced stage, including 22.55% at stage III and 46.41% at stage IV as shown in Table 5. Over the same period the percentage of advanced stage cases have been increased, as Figure 6 shows two main peaks at the year of 2013 and 2016 with 71.43% and 80.00% respectively, however, an average of 65.00% was maintained through the mentioned period which is considered an extremely high percentage.

Table 5: NCCCR Non-Hodgkin Lymphoma Cases 2012-2017

| Year	Number of Patients	Stage I	Stage II	Stage III	Stage IV	Stage III (%)	Stage IV (%)	Advanced Stage (%)	Early Stage (%)
2012	39	5	11	10	13	25.64	33.33	58.97	41.03
2013	35	2	8	8	17	22.86	48.57	71.43	28.57
2014	41	5	8	10	18	24.39	43.90	68.29	31.71
2015	65	6	15	12	32	18.46	49.23	67.69	32.31
2016	55	2	9	12	32	21.82	58.18	80.00	20.00
2017	71	6	18	17	30	23.94	42.25	66.20	33.80
Total	**306**	**26**	**69**	**69**	**142**	**22.55**	**46.41**	**68.95**	**31.05**
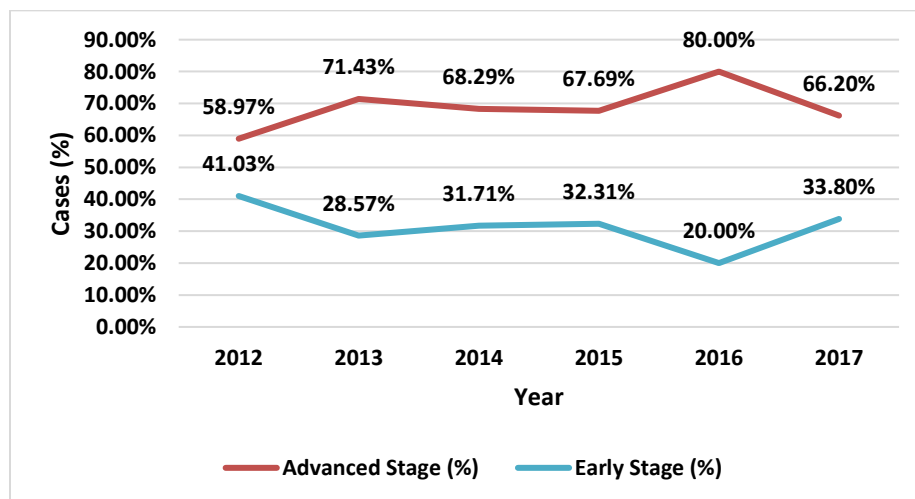
Figure 6: Stage at Diagnosis Trends of Non-Hodgkin Lymphoma 2012-2017

Considering the annual diagnosed cases at each year for each stage, there were a maximum of 6 cases diagnosed with stage I NHL, a maximum of 18 cases diagnosed with stage II, a maximum of 17 cases diagnosed with stage III, while a maximum of 32 cases diagnosed with stage IV at least in one year within the mentioned period. The mean and standard deviation of the annual diagnosed cases with 95% confidence interval were the largest for stage IV with 23.67 and 8.595 respectively as shown in Table 6 which indicates that there is a serious late diagnosis problem of NHL at the NCCCR.

Table 6: Descriptive Statistics of 2012-2017 Non-Hodgkin Lymphoma Cases

	Minimum	Maximum	Mean	Std. Deviation
Stage I	2	6	4.33	1.862
Stage II	8	18	11.50	4.135
Stage III	8	17	11.50	3.082
Stage IV	13	32	23.67	8.595

By comparing the total annual early and advanced stages cases, it is obvious that the later results were always higher. As Table 7 shows, the 35.17 mean and 10.944 standard deviation of advanced stage cases is notably higher than the 15.83 mean and 5.636 standard deviation of the early stage cases.

Table 7: Descriptive Statistics of Annual Non-Hodgkin Lymphoma Staging

	Total Early Stage	Total Advanced Stage
2012	16	23
2013	10	25
2014	13	28
2015	21	44
2016	11	44
2017	24	47
Total	95	211
Mean	15.83	35.17
Std. Deviation	5.636	10.944

3.4. Stage at Diagnosis Benchmarking

In this section, it will be investigated whether the percentage of advanced stage cases at diagnosis for Qatar differs significantly from the percentage of advanced stage cases at diagnosis for other countries such as; England, United States of America (USA) and Canada. This will help identifying the performance level of the Qatari healthcare system with respect to other countries and will help setting a future target.

The least number of recorded Lymphoma cases were in Canada with a total of 7,590 cases including 880 HL cases and 6,710 NHL cases, extracted from the Canadian Cancer Registry Database and covering the period of 2011-2015. While England has recorded 67,311 Lymphoma cases including 8,713 HL cases and 58,598 NHL cases, extracted from the National Cancer Registration and Analysis Service and covering the period of 2012-2016.

On the other hand, USA has recorded the highest number of Lymphoma cases with a total of 111,272 cases including 14,692 HL cases and 96,580 NHL cases, extracted from the Surveillance, Epidemiology, and End Results (SEER) database and covering the period of 2008-2014. The percentages of stage at diagnosis for each Lymphoma type per country is shown in Table 8 and Table 9.

Table 8: Percentages of Stage at Diagnosis for Hodgkin Lymphoma

Country	Years Period	Early Stage (%)	Advanced Stage (%)	Unstaged (%)
England	2012-2016	53.74	29.30	16.96
USA	2008-2014	54.87	40.77	4.36
Canada	2011-2015	53.41	46.02	0.57

Table 9: Percentages of Stage at Diagnosis for Non-Hodgkin Lymphoma

Country	Years Period	Early Stage (%)	Advanced Stage (%)	Unstaged (%)
England	2012-2016	24.84	47.71	27.45
USA	2008-2014	42.50	49.77	7.73
Canada	2011-2015	38.38	58.27	3.35

Based on the previous results, the least percentage of advanced stage cases at diagnosis was for England with 29.30% for HL and 47.71% for NHL as shown at Figure 7, followed by USA with 40.77% for HL and 49.77% for NHL, then by Canada with 46.02% for HL and 58.27% for NHL. Finally, Qatar's percentages were the highest for both Lymphoma types, having 56.48% for HL and 68.95% for NHL. This benchmark indicates that there is a potential achievable improvement for Qatar to pursue.
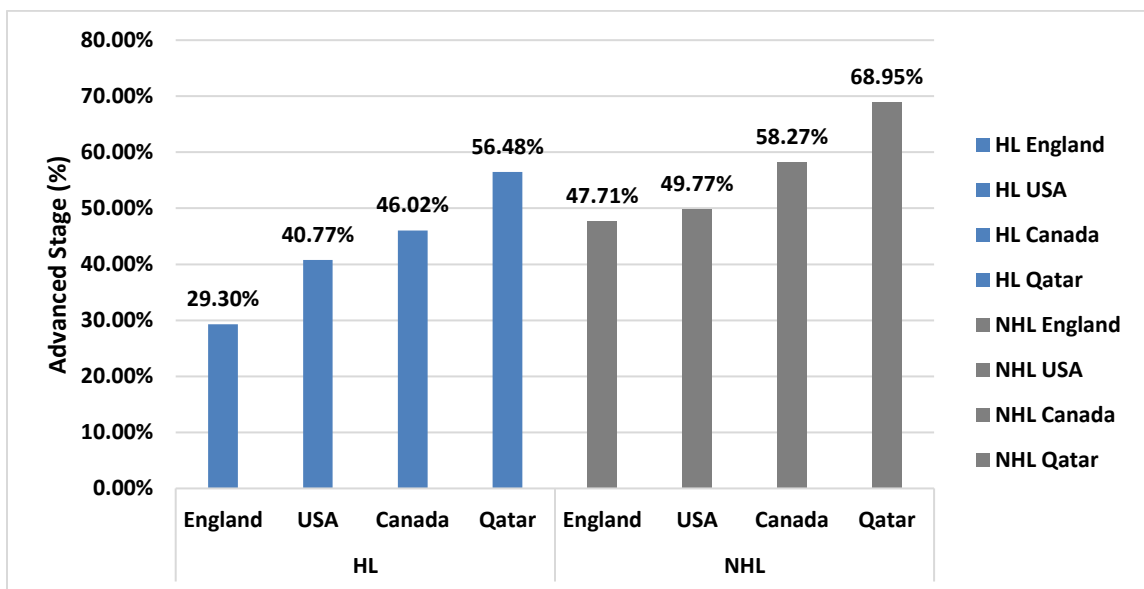
Figure 7: Percentages of Advanced Stage at Diagnosis Cases Benchmarking

3.5. Assessment of Patient Related Factors

In order to be able to achieve early diagnosis for adult Lymphoma patients in Qatar, some patient related factors such as gender, age and nationality were examined, in order to identify potential risk factors among Qatar's population and to assess the existence of any association between the aforementioned patient related factors and stage at diagnosis. Therefore, two hypotheses are formulated as following:

- Null Hypothesis (H_0): Assume no association between a patient related factor and stage at diagnosis.

- Alternative Hypothesis (H_1): Assume association between a patient related factor and stage at diagnosis.

The decision between the two hypothesis will be made according to the P-Value which is set to 0.05. If $P \leq 0.05$, then H_0 will be rejected, however, if $P > 0.05$, then H_0 will not be rejected. Alternatively, Table 10 shows how the P-Value can be interpreted in more detail (Gilchrist & Samuels, 2014).

Table 10: Interpretation of the P-Value

P-Value of the Test	Association	Formal Action	Informal Interpretation
Greater than 0.1	No	Do not reject H_0	No evidence to reject H_0
Between 0.1 – 0.05	No	Do not reject H_0	Weak evidence to reject H_0
Between 0.05 – 0.01	Yes, at 95%	Reject H_0 at 95% confident	Evidence to reject H_0
Between 0.01 – 0.001	Yes, at 99%	Reject H_0 at 99% confident	Strong evidence to reject H_0
Less than 0.001	Yes, at 99.1%	Reject H_0 at 99.9% confident	Very strong evidence to reject H_0

As shown in Figure 8, males have higher incidences to developed HL than females, since 74.07% of the recorded HL cases at the NCCCR were males, while only 25.93% were females. In addition, they are more likely to be diagnosed at advanced stage as only 20 females were diagnosed at advanced stage, while more than the double were diagnosed at advanced stage for males.
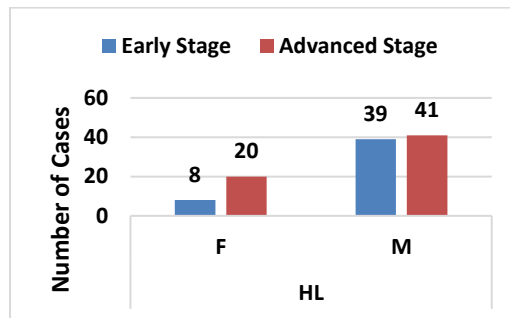
Figure 8: Gender Distribution of Hodgkin Lymphoma Cases

The chi-Square test was conducted to determine the existence of association between two factors; gender and stage at diagnosis. The result from Table 11 indicates that there is no association between gender and stage at diagnosis of HL, because the asymptotic significance value of the Pearson Chi-Square, which is 0.064, is greater than 0.05. However, there is a weak evidence to reject the H_0 and if the sample size is increased, there is a chance that the association becomes significant at 0.05.

Table 11: Stage and Gender Chi-Square Test of Hodgkin Lymphoma

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.436[a]	1	0.064		
Continuity Correction[b]	2.664	1	0.103		
Likelihood Ratio	3.543	1	0.060		
Fisher's Exact Test				0.078	0.050
N of Valid Cases	108				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 12.19.					
b. Computed only for a 2x2 table					

Considering the patients' age factor, it can be noticed from Figure 9 that people aged between 20-39 are most likely to develop HL, especially people aged between 30-39, since the NCCCR data has recorded 17 patients diagnosed with HL at early stage, while 16 patients diagnosed at advanced stage within the mentioned age range. However, The Average age at diagnosis was 40 years old in males and 32 years old in females.

Figure 9: Age Distribution of Hodgkin Lymphoma Cases

Nevertheless, the chi-Square test result in Table 12 indicates that there is no association between the age factor and stage at diagnosis of HL, because the asymptotic significance value of the Likelihood Ratio, which is 0.934, is considerably greater than 0.05. In other words, there is no evidence to reject H_0.

Table 12: Stage and Age Chi-Square Test of Hodgkin Lymphoma

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	1.828[a]	6	0.935
Likelihood Ratio	1.834	6	0.934
N of Valid Cases	108		
a. 6 cells (42.9%) have expected count less than 5. The minimum expected count is 1.31.			

Finally, according to the number of cases per patients' nationality, Figure 10 shows that Middle Eastern Nationalities, including; Bahraini, Jordanian, Lebanese, Omani, Palestinian, Qatari, Syrian and Yemeni, have the highest records of HL cases. Followed by Asian nationalities, including; Bangladeshi, Filipino, Indian, Malaysian, Nepalese, Pakistani and Sri Lankan. Then, African nationalities, including; Egyptian, Moroccan, South African and Sudanese.
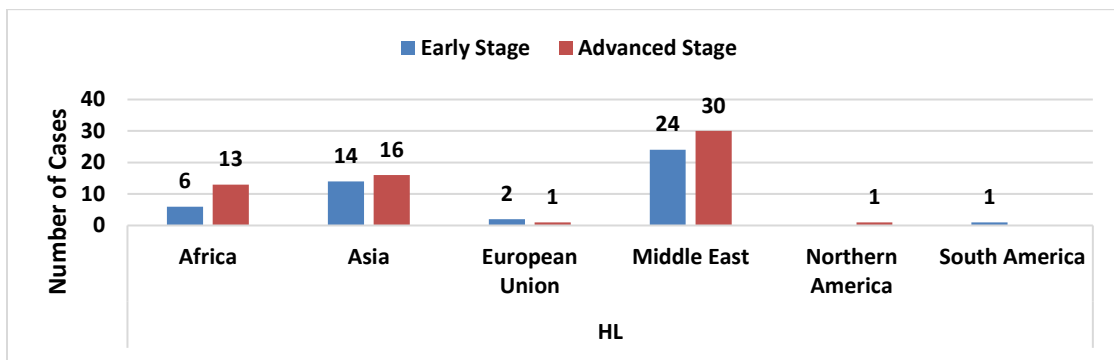
Figure 10: Nationality Distribution of Hodgkin Lymphoma Cases

However, by normalizing the number of cases by considering the total number of people from each nationality which were living in Qatar at 2017, Figure 11 shows that South American nationalities, including; Venezuelan have the highest chance to develop HL followed by Middle Eastern and African nationalities.

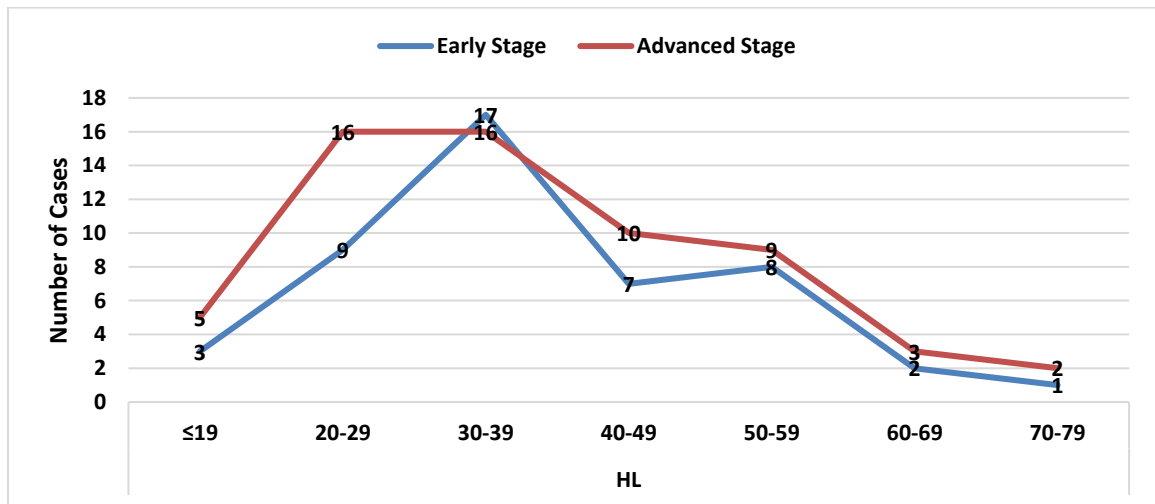Figure 11: Normalized Nationality Distribution of Hodgkin Lymphoma Cases

The chi-Square test result in Table 13 indicates that there is no association between the nationality factor and stage at diagnosis of HL, because the asymptotic significance value of the Likelihood Ratio, which is 0.455, is greater than 0.05. In other words, there is no evidence to reject H_0.

Table 13: Stage and Nationality Chi-Square Test of Hodgkin Lymphoma

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	4.950[a]	6	0.550
Likelihood Ratio	5.724	6	0.455
N of Valid Cases	108		
a. 6 cells (42.9%) have expected count less than 5. The minimum expected count is 0.44.			

For the case of NHL, the same patients related factors including; gender, age and nationality were examined in order to identify protentional ways to achieve early stage at diagnosis for adult Lymphoma patients in Qatar. First, with respect to gender, Figure 12 shows that 70.26% of patients who were diagnosed with NHL were males, out of which 71.63% were diagnosed at advanced stage, thus, it can be concluded that males have higher incidents to develop NHL than females.
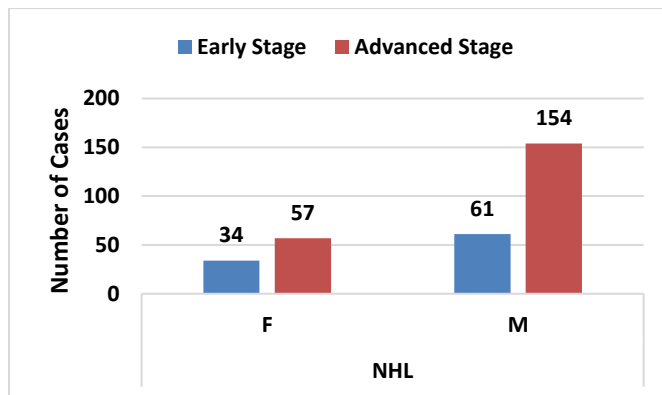
Figure 12: Gender Distribution of Non-Hodgkin Lymphoma Cases

The result from Chi-Square test at Table 14 shows that there is no association between the gender factor and stage at diagnosis of NHL, because the asymptotic significance value of the Pearson Chi-Square, which is 0.120, is greater than 0.05. In other words, there is no evidence to reject H_0.

Table 14: Stage and Gender Chi-Square Test of Non-Hodgkin Lymphoma

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.414[a]	1	0.120		
Continuity Correction[b]	2.012	1	0.156		
Likelihood Ratio	2.371	1	0.124		
Fisher's Exact Test				0.137	0.079
N of Valid Cases	306				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 28.25.					
b. Computed only for a 2x2 table					

By looking at NHL patients' age results in Figure 13, it can be noticed that people aged between 30-69 have high incidents to develop NHL. Especially, people aged between 40-69 are most likely to be diagnosed at advanced stage. However, people less than 30 and greater than 69 years old have much less chances to develop NHL. However, The Average age at diagnosis were 53 years old in males and 51 years old in females.
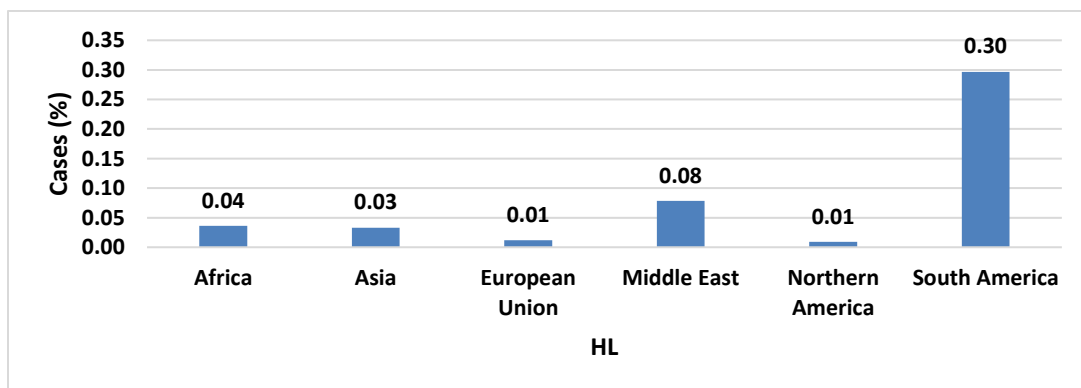

Figure 13: Age Distribution of Non-Hodgkin Lymphoma Cases

However, the chi-Square test result in Table 15 indicates that there is no association between the age factor and stage at diagnosis for NHL, because the asymptotic significance value of the Likelihood Ratio, which is 0.154, is greater than 0.05. In other words, there is no evidence to reject H_0.

Table 15: Stage and Age Chi-Square Test of Non-Hodgkin Lymphoma

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	10.720[a]	8	0.218
Likelihood Ratio	11.932	8	0.154
N of Valid Cases	306		
a. 5 cells (27.8%) have expected count less than 5. The minimum expected count is 0.62.			

Considering the patients' nationality results in Figure 14 for NHL, Asian nationalities have the highest records of NHL cases, including; Bangladeshi, Filipino, Indian, Indonesian, Nepalese, Pakistani and Sri Lankan. Followed by Middle Eastern nationalities, including; Bahraini, Iranian, Iraqi, Jordanian, Kuwaiti, Lebanese, Omani, Palestinian, Qatari, Saudi, Syrian and Yemeni. Then African nationalities, including; Algerian, Cameroonian, Egyptian, Ethiopian, Mauritanian, Moroccan, Nigerian, Somalian, South African, Sudanese, and Tunisian.
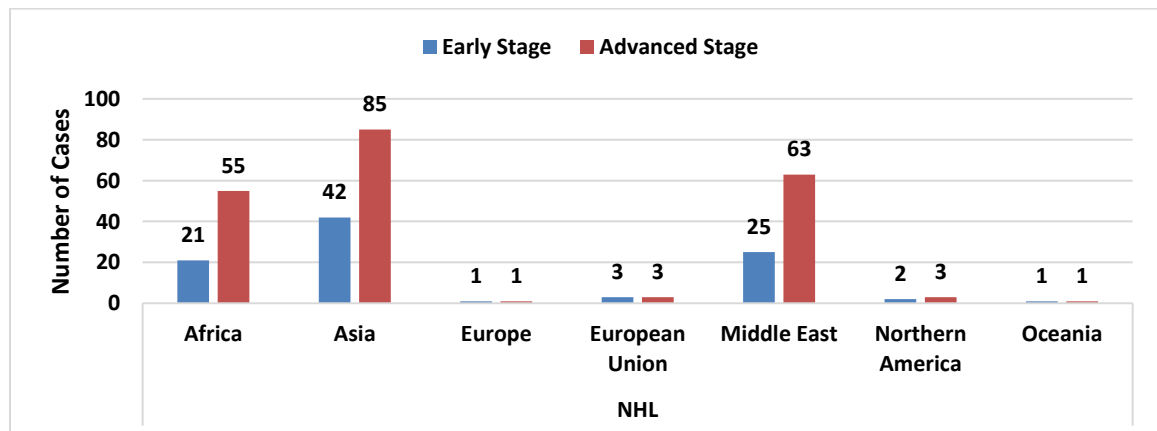
Figure 14: Nationality Distribution of Non-Hodgkin Lymphoma Cases

However, by normalizing the number of cases by considering the total number of people from each nationality which were living at Qatar in 2017, Figure 15 shows that European Union nationalities, including; British, Bulgarian, Czech and Dutch, have the highest chance to develop NHL. Followed by European nationalities including; Bosnian and Swiss. Then, Middle Eastern nationalities.

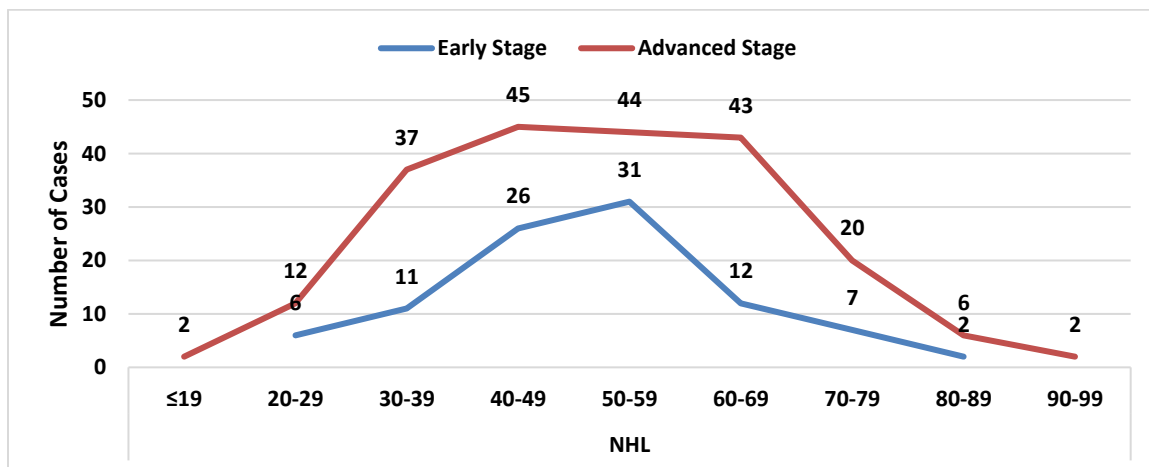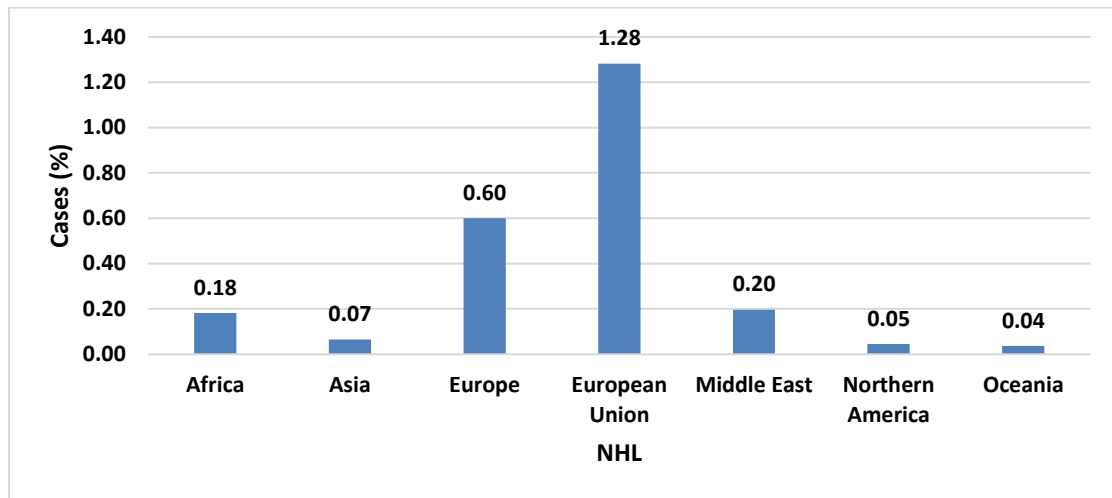Figure 15: Normalized Nationality Distribution of Non-Hodgkin Lymphoma Cases

The chi-Square test result in Table 16 indicates that there is no association between the nationality factor and stage at diagnosis for NHL, because the asymptotic significance value of the Likelihood Ratio, which is 0.875, is greater than 0.05. In other words, there is no evidence to reject H_0.

Table 16: Stage and Nationality Chi-Square Test of Non-Hodgkin Lymphoma

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	3.211[a]	7	0.865
Likelihood Ratio	3.104	7	0.875
N of Valid Cases	306		
a. 8 cells (50.0%) have expected count less than 5. The minimum expected count is 0.62.			

3.6. Effect of Stage at Diagnosis on Patients

There are three main statuses for patients diagnosed with Lymphoma at NCCCR; Deceased, Alive and Lost to Follow UP (LFU). Patients with alive status, doesn't necessary mean positive consequences, as those patients could suffer from long and painful treatment periods. Also, the system would be loaded with following up appointments for large number of patients. Indeed, The LFU patients are those who exited the NCCCR system to seek treatment abroad or who had to return to their home country without finishing their treatment.

By assessing the implications of stage at diagnosis on patients' survival, it is clear from Table 17 that patients who were diagnosed with stage IV HL are most likely to not survive. In fact, the survival curve indicates that patients with stage IV would survive maximum to 2.51 years after being diagnosed with a probability of 0.65 as shown in Figure 16. Yet, there are no sufficient data to indicate how the survival curve will behave for patients with either stage I, II or III at diagnosis.

Table 17: Stage at Diagnosis Vs. Patients' Status for Hodgkin Lymphoma

Patient Status	Early Stage		Advanced Stage	
	I	II	III	IV
Deceased	0	0	0	3
Total	0		3	
Alive	14	21	22	32
Total	35		54	
Lost to Follow Up	5	7	1	3
Total	14		4	
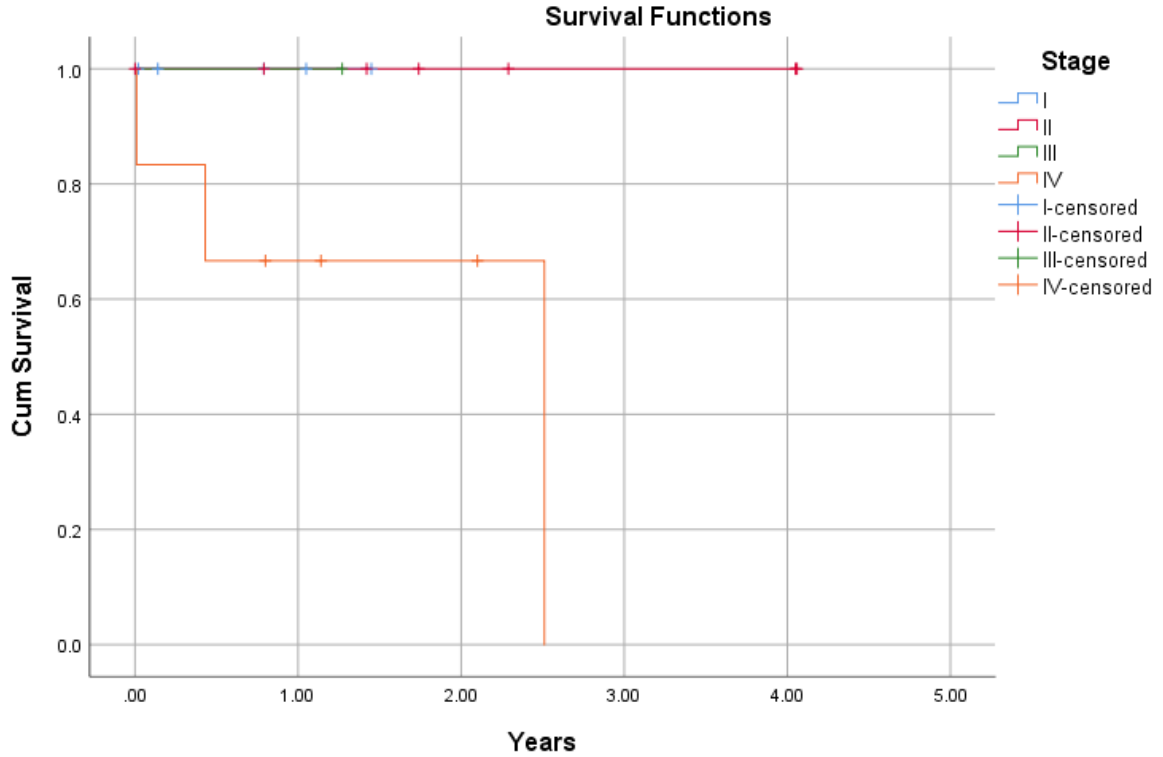
Figure 16: Hodgkin Lymphoma Survival Curve

In order to investigate the equality of survival curves for the different stage levels, three tests were applied as shown in Table 18. Since for all tests the α was greater than 0.05, then it can be concluded that there is no significant difference in survival curves across the stage levels at diagnosis, including stage I, II, III and IV, for Hodgkin Lymphoma.

Table 18: Equality Tests of survival Curves for Hodgkin Lymphoma

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	6.000	3	0.112
Breslow (Generalized Wilcoxon)	4.653	3	0.199
Tarone-Ware	5.403	3	0.145

On the other hand, Table 19 summarize the status of patients with NHL which further proves that patients who were diagnosed with advanced stage such as stage III and stage IV are most likely to not survive. In fact, the survival curve shown in Figure 17 indicates that patients with stage IV would survive maximum to 3.90 years after being diagnosed with a probability of 0.09, while patients with stage III would survive maximum to 4.27 years after being diagnosed with a probability of 0.42.

However, the probability is much higher for stage II being 0.79 for surviving more than 4.00 years after being diagnosed, while for stage I, the probability is 1.00 for surviving more than 5.00 years after being diagnosed. This results highlight the crucial effect of early Lymphoma diagnosis on patients survival and the quality of life they would be living.

Table 19: Stage at Diagnosis Vs. Patients' Status for Non-Hodgkin Lymphoma

Patient Status	Early Stage		Advanced Stage	
	I	II	III	IV
Deceased	0	3	11	32
Total	3		43	
Alive	20	45	47	69
Total	65		116	
Lost to Follow Up	6	21	11	41
Total	27		52	
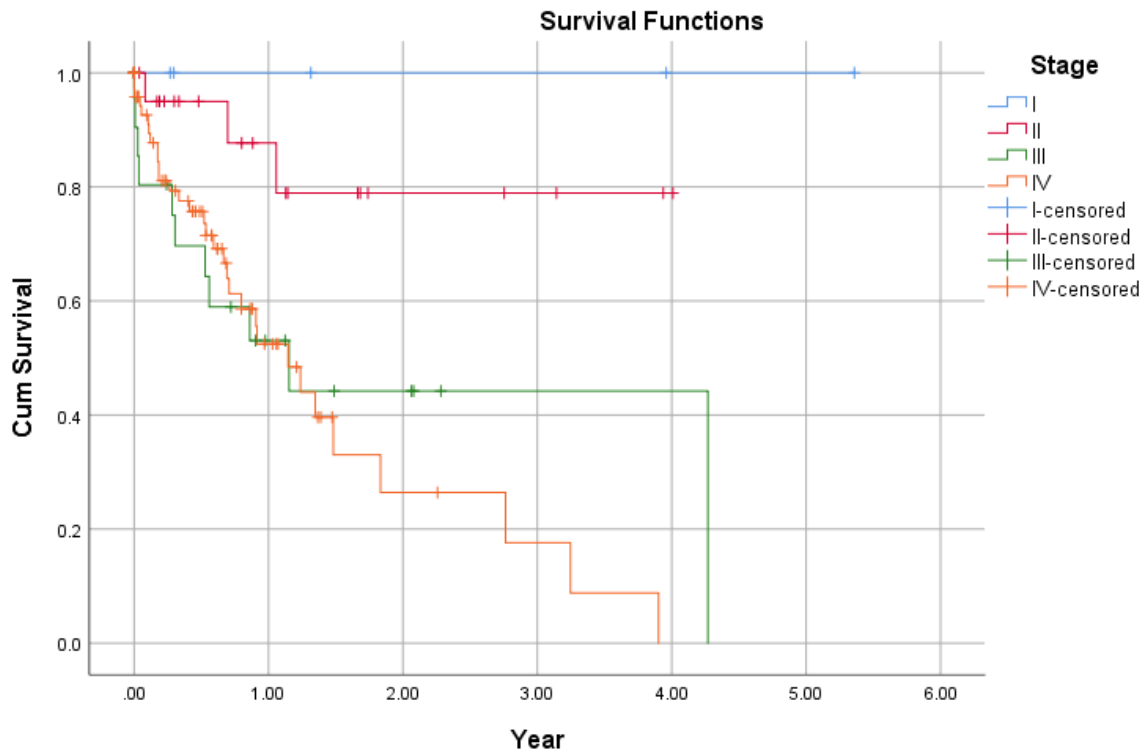
Figure 17: Non-Hodgkin Lymphoma Survival Curve

The same three tests were applied in order to investigate the equality of survival curves for the different stage levels as shown in Table 20, however, all the α was significantly less than 0.05, thus it can be concluded that there is a significant difference in survival curves across the stage levels at diagnosis, including stage I, II, III and IV, for Non-Hodgkin Lymphoma.

Table 20: Equality Tests of survival Curves for Non-Hodgkin Lymphoma

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	14.085	3	0.003
Breslow (Generalized Wilcoxon)	8.501	3	0.037
Tarone-Ware	10.374	3	0.016

3.7. Lymphoma Patients' Pathway Analysis

The pathway of adult Lymphoma patients in Qatar, including HL and NHL, can be described through Figure 18. At the patient interval phase, many patients who are experiencing symptoms are not willing to consult a doctor due to many psychological and economic factors, while others are not recognizing their symptoms at all, therefore, are usually present as emergencies. Even at the primary care interval phase, Lymphoma might not be suspected after a medical examination due to the nature of its symptoms being broad and nonspecific. Indeed, the duration of both the patient and the primary care intervals can highly impact treatment outcomes and survival rate of patients.

All population in Qatar whether nationals, expatriates or tourists, are receiving a universal health insurance and are offered a choice of providers from across the public and private sectors. The governmental healthcare services can be accessed by citizens and residents through a state-issued health card, while private healthcare services can be accessed by obtaining a private health insurance. In fact, many employees are offered a health insurance form their employers.

Hamad Medical Corporation (HMC) was the first governmental and non-profitable healthcare provider in the country. Nowadays, it is the premier healthcare provider which runs a large network of hospitals and ambulances including NCCCR, which is the premier cancer hospital. However, due the growing population, the private healthcare providers have been increasing simultaneously. The services provided by both types of the healthcare providers are free or highly subsidized, as expatriates are likely to pay some of the medical costs.
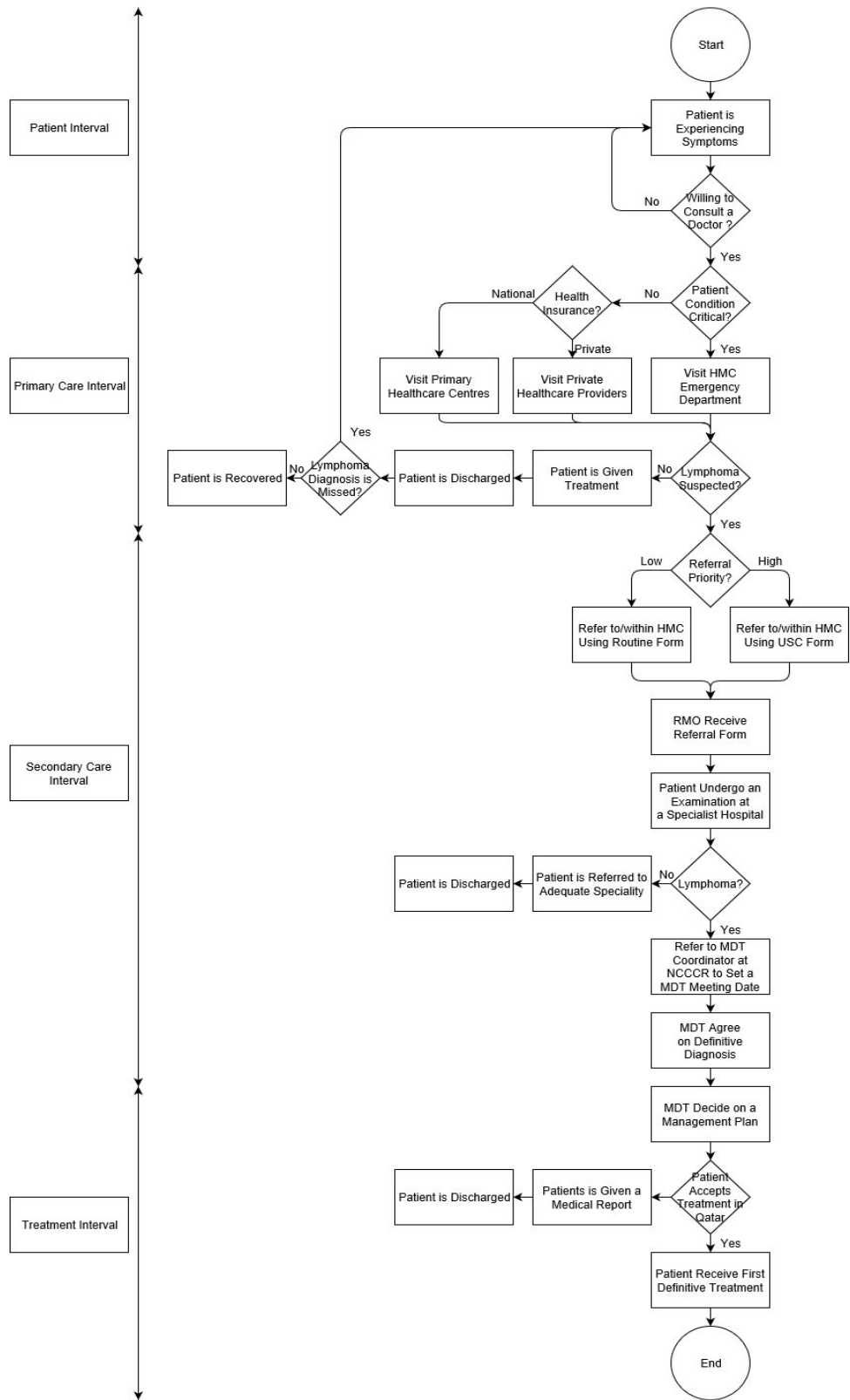
Figure 18: Lymphoma Patients Pathway Flow Chart

The secondary care interval phase starts when a patient who is suspected with Lymphoma is referred to a specialist hospital through one of the following routes; Primary Healthcare Centers (PHCCs), private healthcare providers or internal HMC referrals from other consultants within emergency department. Two types of referral forms could be used; the Urgent Suspected Cancer (USC) form or routine referral form, based on the patient's medical situation. In addition, patients who are returning to Qatar following treatment overseas, could be also referred. All the new Lymphoma patients referrals are managed by the Referral Management Office (RMO).

The next step is to carry out a clinical examination and diagnostic investigations for the patients at the specialist hospital. Those referred using the USC form are seen within 48 hours of referral while others are given an appointment subject to the system availability. In case the results confirm or suspect Lymphoma as a diagnosis, the cases is referred for discussion and/or opinion at the MDT, which is managed by the MDT coordinator at NCCCR. By the MDT discussion meeting, any relevant imaging and pathology are made available for review and a definitive diagnosis including staging is reached in 14 days, regardless of the referral route.

Finally, the MDT decide on an appropriate plan of care, which is discussed later with the patient in an appointment. The outcome of the discussion at the MDT is uploaded onto the system, which enables the referring physician, PHCC or HMC, to review all the patient records, while other referring providers is communicated within a mutually agreed format. The first definitive treatment is given within no more than 14 days after confirming the diagnosis at MDT discussion, regardless of the referral route.

Chapter 4: Improvements for Shortening Lymphoma Diagnostic Pathway

Cancer has a huge impact on patients and those people close to them, such as families and friends. According to the Qatar National Cancer Registry, in 2014, Breast Cancer, Colorectal Cancer, Prostate Cancer, Lymphoma, Leukemia and Lung Cancers, were recorded as the six most common cancers in Qatar, with 17.50%, 10.23%, 6.77%, 6.50%, 5.70% and 5.00% respectively. Therefore, it makes sense to give the highest priority to those cancers with the highest incidence in Qatar.

Hence, the Supreme Council of Health has complied, with the participation of other parties, a management guidelines for; Breast, Colorectal and Prostate Cancers, as to assist in their diagnosis, management, treatment and care. In addition, awareness and screening services were provided for Breast and Colorectal Cancers, while trails for Prostate Cancer are ongoing. The services are delivered by PHCCs and HMC, and have significantly improved referral of people suspected with cancer and treatment outcomes. Therefore, it is time to put more effort for shortening Lymphoma diagnostic pathway.

4.1. Lymphoma Awareness Campaign

Because of the nature of HL and NHL symptoms being broad and nonspecific, there are no widely recommended screening tests for Lymphoma at this time. Indeed screening tests are used to look for a disease in people who have no symptoms and there is no current screening tests which have proven to lower the risk of dying from Lymphoma. Therefore, the best practice is to raise awareness of the disease, its

prevention and early detection that promote the best outcomes for those affected, which eventually will lead to significant reduction of the patient interval phase.

There are many indications that prove the lack of Lymphoma awareness among Qatar Communities, including:

- The NCCCR, which is considered as the premier cancer hospital in Qatar, has no structured efforts in improving awareness of Lymphoma. Furthermore, the late stage at diagnosis levels at NCCCR suggests that because patients have lack of knowledge about symptoms, they mostly assume a simple explanation for their symptoms including; fever, fatigue, etc. and hence neglect them. This suggestion is also confirmed by NCCCR doctors.

- Just recently, PHCC has agreed with the Ministry of Public Health, Hamad Medical Corporation and Qatar Cancer Society to unify the cancer awareness months into one calendar as shown in Figure 19. The announcement was made at a press conference held on December 4th, 2018 and August was the chosen Month for Lymphoma Awareness. This allows centered collaboration on developing the awareness initiatives to achieve maximum positive results.

- The Qatar Cancer Society has never held any campaigns related to Lymphoma since its foundation in 1997, even though, one of their strategic goals is to increase awareness of cancer, prevention methods and early detection. In fact, all their awareness campaigns were oriented about Cervical Cancer, Thyroid Cancer, and Breast Cancer.

Figure 19: Calendar of Cancer Awareness

Therefore, a successful and strong Lymphoma awareness campaign can be initiated through the following proposed steps shown in Figure 20. It is essential to empower population to make the best health choices for themselves and their families.
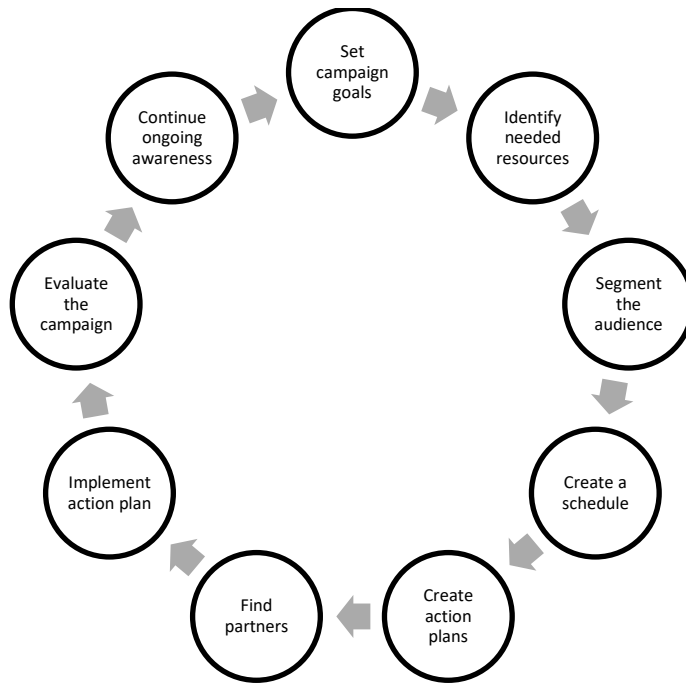
Figure 20: Steps of Creating Awareness Campaign

- **Step 1: Set Campaign Goals:**

Lymphoma is the fourth most common cancer in Qatar; therefore, it is essential to raise awareness of the disease to ensure that everyone knows what to look out for, which in turn will contribute to early Lymphoma detection. The campaign goals could include, but not limited to:

- Increase awareness of Lymphoma signs and symptoms.

- Educate people about Lymphoma high risk factors.

- Encourage people to seek medical consultation if they notice any symptoms.

- Promote the concept of Lymphoma as a curable disease.

- **Step 2: Identify Needed Resources:**

 Awareness campaign requires a lot of resources, such as; identifying a campaign supporter, setting budget, allocating time and producing promotional materials. However, efficiency is important factor while identifying the needed resources in order to be able to reach a maximum number of people with a minimum number of resources. The campaign supporter could be the Ministry of Public Health, which has recently initiated the National Cancer Program. For the campaign budget, even though it is expected to be in Millions, its consequences worth the effort, as the campaign will significantly reduce the burden of Lymphoma on the country, whilst insuring a better service and treatment outcome for the patients.

 The time factor is considered the third needed resource that is essential for a successful campaign, therefore, identifying durations of each event should be made with high level of accuracy. Finally, promotional materials can be produced in many formats such as; brochures, lectures, booklets, videos, logo pins and advertisements. They are considered a key to any campaign, because they allow the receiver to walk away with the intended information in their hands. An example of the type of information that would be shared through the promotional materials is shown at Figure 21.

Figure 21: Information Shared Through Marketing and Promotional Materials

- **Step 3: Segment the Audience:**

    It is essential to determine the targeted group of the population by the campaign. According to the NCCCR data analysis results, Lymphoma highest case records were for male, aged between 20-69 and Middle Eastern, Asian or African natives. Therefore, the campaign main challenge is to overcome the language barrier and cultural diversity. That is mainly due huge inflow of expatriates who neither speak Arabic nor English like Qataris, thus, the awareness message must be appropriate culturally and linguistically.

    In fact, most Asian and African countries have many official languages, beside many other dialects, thus, communication could be even hard between expatriates from the same country. The most common languages among the aforementioned countries are highlighted in Table 21 and Table 22, which confirm the need of providing the awareness in the audience slang language. In this case, The Public Relations Department of the Ministry of Interior could collaborate by providing translators in different languages.

- **Step 4: Create a Schedule:**

    Planning a specific schedule of the awareness campaign events is the next step after identifying the campaign goals, resources and audience, which dependents on the awareness campaign type, being passive or active. A passive campaign uses hard promotional materials to raise awareness, while an active campaign may use lectures that present information directly to the targeted audience. Yet, a combination of both campaign types would have the best impact on the audience. Finally, the campaign should be scheduled on August, which is the Blood Cancer awareness month according to the unified calendar of the cancer awareness.

Table 21: Most Common Languages Among Asian Countries

		Nationality							
		Bangladeshi	Filipino	Indian	Indonesian	Malaysian	Nepalese	Pakistani	Sri Lankan
Language	Bahasa Indonesia				✓				
	Bengali	✓		✓					
	Hindi			✓					
	Maithili						✓		
	Malayalam			✓		✓			
	Sindhi			✓				✓	
	Tagalog		✓						
	Tamil			✓		✓			✓
	Telugu			✓		✓			
	Urdu			✓				✓	
	Punjabi			✓		✓		✓	

Table 22: Most Common Languages Among African Countries

Language		Nationality										
		Algeria	Cameroon	Egypt	Ethiopia	Mauritania	Morocco	Nigeria	Somalia	South Africa	Sudan	Tunisia
	Afrikaans									✓		
	Amharic				✓							
	Arabic	✓		✓		✓	✓		✓		✓	✓
	Berber						✓					
	English		✓					✓		✓	✓	
	French		✓									
	Northern Sotho, Sotho, Southern Ndebele, Swazi									✓		
	Tamazight	✓										
	Tsonga, Tswana, Venda, Xhosa, Zulu									✓		

Step 5: Create Action Plans:

After creating a schedule of events for the awareness campaign, it is time to create a detailed action plan for each specific event. The action plan should include, but not limited to the following:

- Where the event will take place.

- The specific date and time of the event.

- How to advertise for the event.

- When to start advertising for the event.

- The type of activities that will take place during the event.

By this time, the delivery method of the campaign should be made clear, whether it will be conducted through lecturing and distributing brochures at workplace or through visiting workers at their accommodations. In fact, the Industrial area could be an ideal place for the events due to the high number of Asian communities living there.

In addition, information booths could be placed at some HMC's hospitals and popular attractions as shopping malls in order to reach Qataris and African nationalities. A social media campaign could be started alongside to strengthen the campaign effect. Indeed, it is essential to place any required orders for promotional materials at the earliest to ensure they would be available before the awareness campaign starts.

- **Step 6: Find Partners:**

Creating a strong partnerships with members in the community can make the awareness campaign much easier, mostly when a larger audience is more accessible through partners. Such community engagement is essential to improve the health of the

population as they help in sustaining the awareness campaigns and promoting efficient utilization of existing resources.

Examples of the campaign's partner includes community leaders such as municipalities, religious communities and sports authorities. In addition to universities, banks, hotels, telecommunication companies, airlines companies, shopping malls and many other private companies. Undoubtedly, partners will be willing to work together in order to meet the community needs.

- **Step 7: Implement Action Plan:**

The following step is to implement the action plan previously developed for accomplishing the targeted goals. Any changes in the plan is acceptable as the program evolves as long as it is necessary, justifiable and applicable. However, it is important to maintain the ability to quantify the effect of the awareness campaign efficiently.

- **Step 8: Evaluate the Campaign:**

Indeed, assessing and measuring the targeted goals continuously will make the final evaluation process of the awareness campaign much easier. This include feedback from audience and partners through surveys, in addition to identifying common trends over the entire campaign's events. In fact, reviewing the success of individual events will contribute significantly to achieving the campaign's goals and consequently its success.

An example of the needed information for campaign's evaluation include reports for incidence numbers and utilization of the supporting healthcare systems. Certainly, a standardized assessment criteria is the best way to comprehensively assess the performance of the awareness campaign and to enable continuous improvement.

- **Step 9: Continue Ongoing Awareness:**

The effectiveness of the awareness campaign are at most when they are part of a continuous program. Therefore, the schedule peak should be in August, however, smaller events should be carried out through the remaining months in order to make Lymphoma awareness a part of the community. Since an ongoing program will require more resources, it is advised to adapt this principle only in early lifetime of the awareness campaign, until a desirable state of the Lymphoma awareness is reached.

4.2. Lymphoma Education Program for General Practitioners

Running a program of events which aims to educate, train and support GPs in spotting the signs of Lymphoma quickly and confidently in order to refer patients at the right time, is an effective solution to overcome late referral. In turn, it will encourage early Lymphoma detection, improve treatment outcomes and significantly reduce the primary care interval phase.

With the present and future challenges faced by Qatar's population, such education programs can be directed to satisfy the continuous community health needs assessment. As a result, a health workforce that is able to deliver a high performance level will be developed. This proposed solution will also help in delivering more effective medical care services for the population by ensuring that the right level and mix of skills are available at the required locations in the healthcare system and that it matches the individual needs.

A strong education program may include education lectures, workshops, online courses, interactive seminars, case studies and a network gathering opportunities for GPs from all types of healthcare providers, which covers aspects of Lymphoma diagnosis, treatment and care. In fact, most GPs are aware that Lymphoma may present a wide range of symptoms, each may has a different medical explanation, therefore the education program is essential to improve GPs' Lymphoma detection ability.

During the program, the light shall be spotted on the combination of symptoms and signs that may suggest Lymphoma and therefore, requires full examination, further investigation and possible referral. The alerting symptoms include; fatigue, bleeding, recurrent infections, night sweats, bone pain, fever, weight loss, abdominal pain, generalized itching, lymphadenopathy, breathlessness, splenomegaly and bruising.

In addition, the program will include a description of the investigation tests that could be used in case of suspected Lymphoma including; full blood count, plasma viscosity, blood film and erythrocyte sedimentation rate, ultrasound, computed tomography or biopsy. Moreover, risk factors, Lymphoma updates, fast diagnose tips, new advances in Lymphoma care, as well as latest techniques and trials will also be included in the program and discussed.

The education program will be delivered by a multidisciplinary team of experts through interactive case studies, panel discussions and clinical lectures. Indeed, the presenters will work collaboratively with GPs to shape and deliver a high quality of Lymphoma education and innovative training. The most important factor to encourage attendance is through having a convenient and accessible location, which should be considered as the program is being planned.

Since the GPs have a vital role in the early recognition of Lymphoma, such education initiatives is essential once a year to increase GPs awareness and to improve their diagnostic skills of Lymphoma. The networking opportunity could be for one day or for several days depending on the program content and intensity. The outcome of the program is that GPs will be better placed to diagnose Lymphoma early, refer earlier and above all be more informed in managing a patient holistically.

4.3. Effectiveness of the Proposed Improvements

A combination of both awareness campaign and GPs education program will be most effective as each will work independently on reducing a specific interval phase of the Lymphoma diagnostic pathway. In other words, the patient interval phase will be reduced by conducting an awareness campaign of lymphoma symptoms and risk factors. Alongside, the primary care interval phase will be reduced by initiating an education and training program for GPs to improve their detection skills and referral behavior. Eventually, the ultimate goal will be achievable, which is to reduce the number of Lymphoma cases that is diagnosed at advanced stage.

The aforementioned improvements have been proposed because they are capable of overcoming the source of delay summarized in Table 23. Since patients with suspected Lymphoma are mainly receiving their definitive diagnosis at the secondary care interval phase, then, the length of patient and primary care interval phases must be reduced in order to reduce the Lymphoma diagnosis delay.

Table 23: Source of Delays Summary with Proposed Improvements

Targeted Lymphoma Diagnostic Intervals for Reduction	Source of Delay	Proposed Improvement
Patient Interval Phase	• Patients cannot identify the symptoms. • Psychological and emotional barriers (Fear, Worries, Trust, etc.). • Patients-related factors (Gender, Age, Nationality, etc.). • Socioeconomic factors (Income Level, Education Level, etc.).	Lymphoma Awareness Campaign
Primary Care Interval Phase	• Gatekeeper role of GPs at primary care. • Lack of GP's knowledge which results to multiple medical consultation. • Lack of availability and/or accessibility to appropriate diagnostic tests. • Late referral behavior of GPs.	Lymphoma Education Program for General Practitioners

The Lymphoma awareness campaign will help in increasing the awareness of Lymphoma symptoms and risk factors, so patients would know what to look for and be able to distinguish which symptoms matter the most. In addition, it will encourage people to early seek medical consultation if they notice any symptoms and promote the concept of Lymphoma as a curable disease, therefore any psychological concerns would be eliminated.

Also, through the patients-related factors analysis, the targeted audience of the campaign would be identified. Consequently the delivery method of the campaign would be better planned for, in order to achieve the highest impact. Finally, the Lymphoma Awareness Campaign would overcome the socioeconomic factors because it would be delivered on a national level, hence, it will reach population from all income and education levels. Besides that, there is no need to concern about the medical cost as all

the provided services in Qatar are free or highly subsidized as expatriates are likely to pay some of the medical costs.

On the other hand, the Lymphoma education program for GPs would work thoroughly to highlight the importance of GPs role in early detection of Lymphoma. Hence, they are encouraged to listen more to their patients' needs and to request further examinations if they felt a need for. In addition, GPs will no longer exercise the unjustifiable 'wait-and-see' behavior because their observational skills will be improved through the provided education on the combination of signs and symptoms.

Through Lymphoma education program, the current and latest investigation tests will be described, thus GPs will be up-to-date with the latest techniques and they could request the needed equipment from top management in order to be able to provide a better health care service for the patients. Furthermore, the responsiveness of the GPs will be improved and the referral to secondary care will be faster, consequently, promoting early Lymphoma diagnosis.

Based on previous discussion and literature review, the awareness campaign are generally considered a very effective tool. It can greatly increase chances of early cancer detection and treatment by encouraging patients to ask for a medical consultation at early stages once the symptoms are onset, sometimes even earlier. For this reason, it is extremely important for Qatar Population to be aware of the signs and symptoms of Lymphoma. The effectiveness assessment of the proposed Lymphoma awareness campaign can be concluded from Table 24.

Table 24: Cancer Awareness Campaigns from The Literature Review

Cancer Type	Country	Effectiveness
Breast	Sweden	After a follow-up period of 5 to 13 years, mortality rate was reduced by 29% for women aged 50-69 years and by 13% for women aged 40-49 years.
Lung	United Kingdom	The percentage of cancers identified in stages I or II increased from 11% to 19%
Colorectal	England	The awareness campaign caused a 10% increase for one month in presentation rates to GPs

On a national level, awareness campaigns and screening services for Breast and Bowel Cancers was launched in 2015 to encourage symptoms awareness and early detection for Qatar's population. Nowadays, achieving early stage at diagnosis has proven to be associated with nearly 100% survival rate for Breast Cancer and 90% for Bowel Cancer. Such results confirm the capability and promise effectiveness of Lymphoma awareness campaign in Qatar.

In 2018, a total of 30 Breast Cancer awareness lectures across Qatar was provided, some of them were conducted as part of an awareness event, with around 950 attendances, during which the disease was introduced, its symptoms, different stages and how early can increase survival rate. Other activities conducted throughout awareness booths in different locations, which considered as a good platform to interact with people.

While for Bowel Cancer, a key global initiative named "Movember", was held during November 2018, to raise awareness of men's health issues and to offer an opportunity to reach out for the community to continue raising awareness of Bowel

Cancer. Therefore, with such a solid experience for Qatar in providing health awareness campaigns, it would be easier to initiate the needed Lymphoma awareness campaign.

The education program for GPs has also proven its effectiveness through the previous discussion and literature review. It has the ability to greatly improves GPs detection ability of the disease, speed referrals, as well as, keep them update with the recent researches and clinical procedures. For this reason, it is extremely important for GPs within Qatar to be offered such opportunities to meet with expert teams and share knowledge. The effectiveness assessment of the proposed Lymphoma education program for GPs can be concluded from Table 25.

Table 25: Cancer Education Programs from The Literature Review

Cancer Type	Country	Effectiveness
Skin	United Kingdom	Significant improvement in GPs' diagnostic ability of two study groups from 63% and 55% to 76% and 62%.
Lymphoma	Canada	Significant change in questioning and screening behavior of GPs
Breast	Iran	Educational intervention on 130 female employees of Zahedan University of Medical Sciences has confirmed a positive effect, including knowledge increase of breast cancer preventive and early diagnosis behaviors

On a national level, the NCCCR has recently organized the first masterclass in breast cancer management which was held in Doha on 28 and 29 April 2017. The networking opportunity has gathered more than 300 experts including oncologists, pathologists, gynecologists, surgeons and physicians from PHCC and private healthcare

providers. The level of attendees reflect the high interest in such education opportunities, where many participants attend to improve their knowledge and diagnostic skills.

At the same event, participants has discussed through lectures and case studies, the newest techniques in breast cancer management, debated the latest cancer research and reviewed the best practices from local, regional, and international healthcare institutions. This unique masterclass aimed to expand participants' knowledge base with the ultimate goal of improving breast cancer care standards, saving lives and enhancing quality of patients life.

In order to provide the best patient care, the Ministry of Public Health has applied a very essential policy through forcing Continuing Medical Education (CME) and Continuing Professional Development (CPD) for renewing the medical licenses. Meaning that each healthcare professional must invest some time on educational opportunities, including peer-reviewed learning modules in text, video, or audio formats, to extend their clinical knowledge and skills. Accordingly, points are accumulated until a predefined points level is reached, after which the healthcare professional would be eligible for renewing their medical license.

Another education initiative in Qatar is the annual breast cancer conference which also promote medical knowledge and information sharing amongst health professionals by offering a comprehensive range of sessions, including the latest developments in breast cancer care in the Middle East and worldwide. Therefore, it can be concluded that Qatar is a leader in hosting and providing successful education initiatives, however, it is time to put more effort on Lymphoma education initiatives.

4.4. Cost Benefit Trade-Off

Lymphoma is a very costly disease due its effect on patients' health, emotions, time, relationships and financial situation, even though in Qatar, the medical services are considered totally free or highly subsidized. The previously proposed improvements are aiming to diagnose Lymphoma as early as possible, which will save more lives and will reduce the large cost of treatment at advanced stages. On the other hand, the resources are scarce and sending more potential patients to the secondary care will increases the cost. That is why there is a need to balance the trade-off between the costs and benefits of the proposed improvements.

- **Associated costs of the proposed improvements:**

  1. Staffing and wage costs:

  This category includes recruiting team coordinating implementation of the Lymphoma awareness campaign and its member, in addition to recruiting specialist MDT for providing the GPs' Lymphoma education program. Furthermore, recruiting new staff at HMC including; MDT coordinators, patient pathway coordinators, booking assistants and clinical nurse specialists, in order to manage the increase in patients flow into secondary care, along with Lymphoma registry staff to keep records of Lymphoma cases.

  2. Operating expenses:

  Such expenses include costs of running the Lymphoma awareness campaign, providing the GPs' Lymphoma education program and the research program at HMC. Indeed, the operating expenses will cover the needed resources throughout implementation of the proposed improvements such as rents, equipment, marketing, etc.

3. Capital costs:

The capital costs category compromise mainly of repairing or expanding the HMC and PHCs in order to increase the current capacity of patients and to offer more space for the events that might take place which are associated with the proposed improvements. In addition to information and communication technology capital costs, which is essential to have a more effective and efficient healthcare system.

- **Associated benefits of the proposed improvements:**

1. Achieve early Lymphoma diagnosis:

Early diagnosis of Lymphoma can greatly increases the chances for successful treatment, in addition to reduces patients' suffer from having longer treatment periods. There are two major components of early diagnosis; awareness campaign to promote knowledge about the disease's symptoms which encourage the patient to take prompt actions that lead to early diagnosis, in addition to GPs' education program which have a great impact on the disease and can improve their detection ability. Some early signs of Lymphoma include lumps, fatigue, loss of appetite, fever, sores and abnormal bleeding.

2. Increase survival rate:

Hodgkin's lymphoma is highly treatable, especially when diagnosed at early stages. According to the American Cancer Society, the 5-year relative survival rates for Hodgkin Lymphoma when first diagnosed is 92% for stage I and 93% for stage II, while for patients with stage III and stage IV, the survival rate is lower, being 78% only. The 5-year survival rate for all stages combined is about 87%.

On the other hand, the overall 5-year relative survival rate for Non-Hodgkin Lymphoma is 71% according to the American Cancer Society, however, the survival rates can vary widely for different subtypes and stages. For example, the 5-year relative survival rates for Diffuse large B-cell Lymphoma when first diagnosed is 72% for stage I and stage II, while for patients with stage III and stage IV, the survival rate is much lower, being 55% only. The 5-year survival rate for all stages combined is about 63%.

3. Reduce treatment costs:

Indeed, treating advanced stages for some cancer types have proven to be associated with a significant increase in costs, which is typically due expensive procedures such as surgeries, chemotherapies, drugs radiation therapies and lap tests. Therefore, it can be concluded that early Lymphoma diagnosis could significantly reduce Lymphoma burden on the Qatar's economy. However, available data are generally limited to retrospective considerations of hospital-based direct treatment costs with respect to stage at diagnosis for either Qatar or other countries.

- **Final Value of the proposed improvements:**

Overall, such improvements are essential to raise the standards of Lymphoma care in order to achieve the Qatar's National Vision 2030, which include having a comprehensive world-class healthcare system whose services are accessible and affordable to the whole population. in addition to having a skilled national workforce who are capable of providing a high quality healthcare services.

Chapter 5: Conclusion

The healthcare system standards' in Qatar are generally Excellent. In fact, it has been ranked the first in the Middle East and the 13th in the world by the 2017 Legatum Prosperity Index. With the ultimate goal of reducing the cancer burden, while maintaining the high standards of cancer care services, The National Cancer Strategy has been launched in May 2011 by Her Highness Sheikha Moza bint Nasser and the Minister of Public Health.

Consequently, The Ministry of Public Health, under Qatar's National Cancer Program and in accordance with the country's National Health Strategy 2011-2016, has initiated awareness and screening services for Breast and Colorectal Cancers, which were ranked at 2014 as the first and second most common cancers in Qatar. There is not yet sufficient evidence to warrant screening for other cancer sites. However, trials are ongoing for Prostate Cancer which was ranked as the third most common cancer in Qatar.

Therefore, it was time to put more efforts in studying the diagnostic pathway of Lymphoma which was ranked as the fourth most common cancer in Qatar at the same year. By analyzing a sample of 414 adult Lymphoma cases covering the period of 2012-2017, including 108 HL cases and 306 NHL cases that were extracted from NCCCR database, a basis for understanding the sources, extent, and root causes of Lymphoma diagnostic delays was provided.

It was found that there is a serious late diagnosing problem of Lymphoma patients. In fact, 56.48% of Hodgkin Lymphoma cases and 68.95% of Non-Hodgkin Lymphoma cases were diagnosed at advanced stage throughout the mentioned period. Accordingly, Qatar's advanced stage at diagnosis levels were found to be the highest when benchmarked with other countries such as; England, USA and Canada, having (29.30%, 47.74%), (40.77%, 49.77%) and (46.02%, 58.27%) respectively for Hodgkin Lymphoma and Non-Hodgkin Lymphoma.

In addition, it was found that Lymphoma incidence was generally higher, for both Hodgkin and Non-Hodgkin Lymphoma, for male than females as shown in Figure 22 and for middle aged as shown in Figure 23. Moreover, the number of case records were the highest for Middle Eastern, Asian or African natives as shown in Figure 24.

However, by normalizing the number of cases by considering the total number of people from each nationality which were living in Qatar at 2017, Figure 25 shows that European Union nationalities, including; British, Bulgarian, Czech and Dutch, have the highest chance to develop Lymphoma, including both Hodgkin and Non-Hodgkin Lymphoma. Followed by European nationalities including; Bosnian and Swiss. Then, South American nationalities, including; Venezuelan and Middle Eastern nationalities including; Bahraini, Iranian, Iraqi, Jordanian, Kuwaiti, Lebanese, Omani, Palestinian, Qatari, Saudi, Syrian and Yemeni.
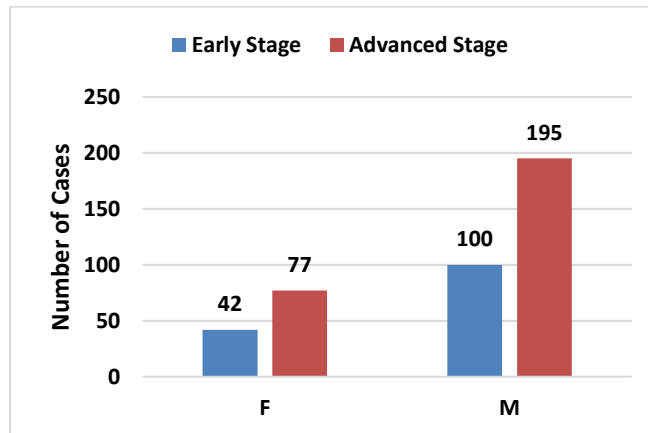
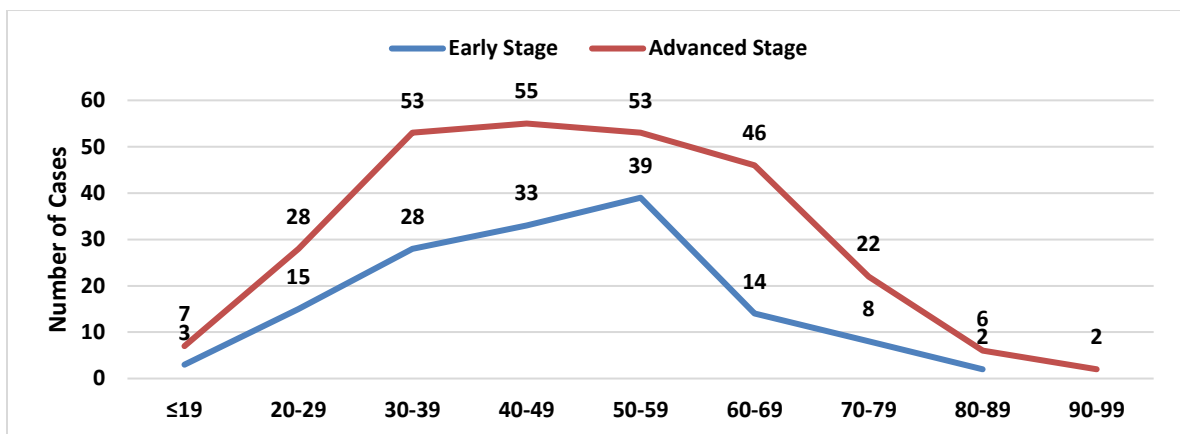Figure 22: Gender Distribution of All Lymphoma Cases

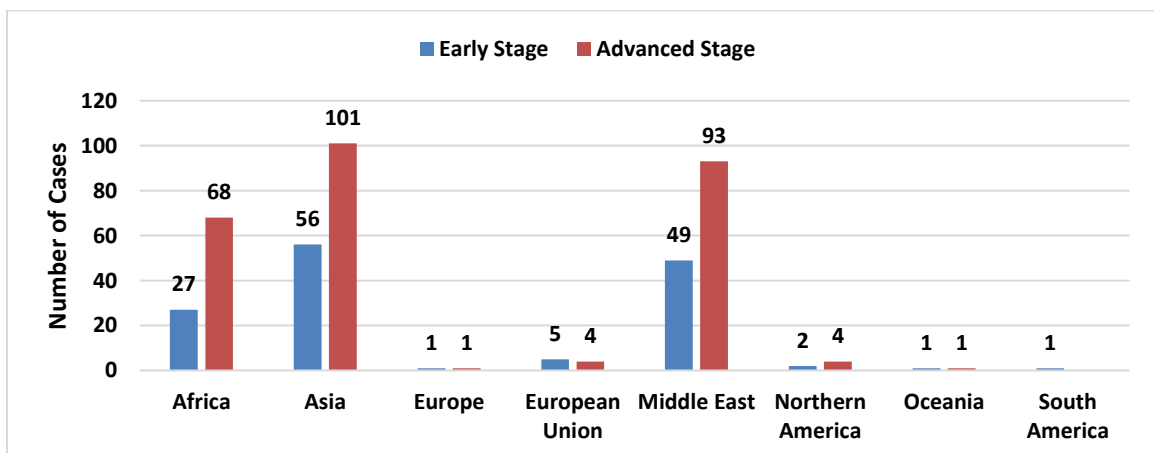Figure 23: Age Distribution of All Lymphoma Cases

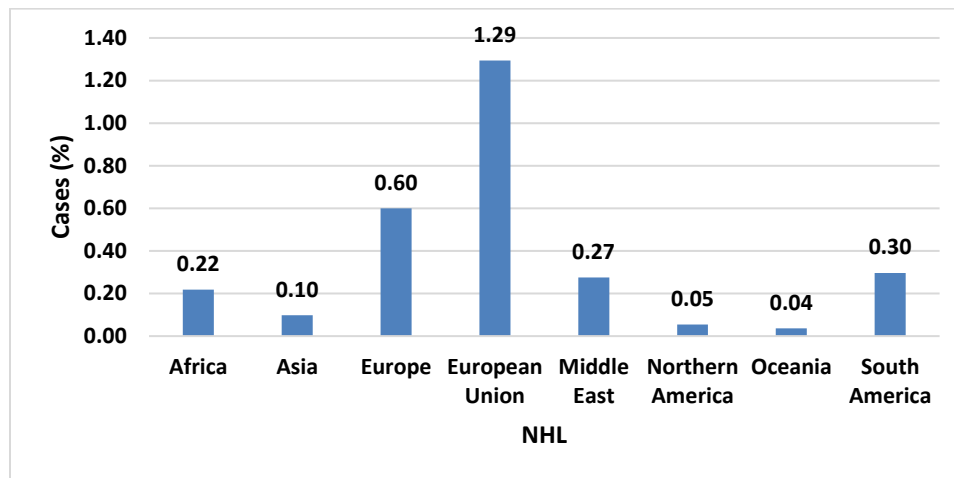Figure 24: Nationality Distribution of All Lymphoma Cases

Figure 25: Normalized Nationality Distribution of All Lymphoma Cases

Furthermore, it was found that there is no association between the previously highlighted patient-related factors including; Gender, Age and Nationality, and diagnosis stage. That is because such factors are not conclusive as the population of Qatar is not homogeneous in terms of gender, age and nationality.

Indeed, Qatar's population mix has encountered many changes in the past decades due to a huge influx of laborers. In fact, according to the Ministry of Development Planning and Statistics, out of the total economically active laborers in 2017, there were 5.07% Qatar nationals, while the remaining 94.93% were non-Qatar nationals, being mostly from Asia and Africa.

Therefore, it is important to assess other factors like socioeconomic factors including; income level, education level, occupation, marital status, etc. which are associated with diagnosis delay. The findings of such factors could be crucial for effective system interventions, facilitate clinical management, in addition to improve Lymphoma detection. Unfortunately, NCCCR does not collect this data from the patients, therefore, the socioeconomic factors was not assessed in the research.

In addition, it was found that the late diagnosis of Lymphoma has significantly reduced patients' survival probability. Actually, the survival curve indicates that patients with stage IV Hodgkin Lymphoma would survive maximum to 2.51 years after being diagnosed with a probability of 0.65. On the other hand, Non-Hodgkin Lymphoma patients with stage IV would survive maximum to 3.90 years after being diagnosed with a probability of 0.09, while patients with stage III would survive maximum to 4.27 years after being diagnosed with a probability of 0.42.

Also, patients with suspected Lymphoma were mainly referred to a specialist hospital through Primary Healthcare Centers, Hamad Medical Cooperation Emergencies and Private Healthcare Providers, by using either routine referral form or urgent suspected cancer form. Then, some clinical examination would be carried on and in case the results confirms Lymphoma as a diagnosis, the case would be referred to the MDT coordinator in order to set a MDT Meeting where the diagnosis is confirmed and a management plan is suggested.

Raising awareness of the symptoms among Qatar's population through Lymphoma awareness campaigns and educating GPs on fast detection and referral through Lymphoma education programs are proposed as to be the best practices for promoting fast referral and early Lymphoma diagnosis. Currently, there is no widely recommended screening tests for Lymphoma because no screening test has proven to lower the risk of dying from Lymphoma.

A strong Lymphoma awareness campaign can be initiated through the proposed nine steps including; setting campaign goals, identifying needed resources, segmenting the audience, creating a schedule, creating action plans, finding partners, implementing action plans, evaluating the campaign then continuing with ongoing awareness. The campaign should be scheduled on August, which is the Blood Cancer awareness month according to the unified calendar of the cancer awareness. And it is most important for the awareness message to be appropriate culturally and linguistically.

The Lymphoma education program may include lectures, case studies and seminars, through which the light is spotted on the combination of symptoms in order to further improve GPs knowledge and diagnosis skills. In addition, risk factors, Lymphoma updates, new advances in Lymphoma care, as well as latest techniques and trials would be covered. As a result, a health workforce that is able to deliver a high performance level with the present and future challenges faced by Qatar's population would be developed.

The proposed improvements will generate many benefits, such as achieve early lymphoma diagnosis, increase survival rate and reduce the large cost of treatment at advanced stages. On the other hand, they will add additional cost into the system, including; staffing and wage costs, operating expenses and capital costs. That is why there is a need to balance the trade-off between the costs and benefits of the proposed improvements. However, such improvements are essential to raise the standards of Lymphoma care and to achieve the Qatar's National Vision 2030.

Chapter 6: Future Recommendations

As a future recommendation, it is necessary to collect full health information about the population into a centralized electronic system, which will allow an effective recording and integrated monitoring. This is mainly because Qatar has a unique population demographic with a transient expatriate population posing a continuous challenge and because Qatar continue to host major international events such as FIFA World Cup 2022.

Therefore, an integrated system is crucial to enable early recognition of key health problems, occurrences rate, emerging and re-emerging threats and to monitor public health challenges. Moreover, the system will be accountable for identifying Qatar's health profiles and to connect it with regional and global units.

By engaging with community members from various sectors to identify exact health needs of the population and designing effective interventions, the community resources will be allowed to utilize efficiently. Hence, a formal response mechanism should be recognized in order to identify the success and performance of local health initiatives and improvement opportunities.

Finally, it is important to define stakeholders' roles, establish a hierarchy of designated leadership and decision makers, in addition to emphasize a clear reporting and escalation processes, by developing a full governance and legislative framework across the healthcare system. Governance is essential to overcome intra and inter sectoral barriers, ensure the ownership of responsibilities and to enable the implementation of health policies.

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