LYMPHOMA
COALITION
Worldwide Network of
Lymphoma Patient Groups

2019 REPORT CARD
ON LYMPHOMAS

AGE-RELATED LYMPHOMA PATIENT EXPERIENCE

About

Lymphoma Coalition

The Lymphoma Coalition (LC), a non-profit organisation, was formed in 2002 and incorporated in 2010 with the express purpose of facilitating lymphoma patient organisations around the world to form a community that could support one another's efforts in helping patients with lymphoma receive the best care and support. LC is currently made up of 82 patient organisations from 52 countries.

Vision

Equity in lymphoma outcomes across borders.

Mission

Enabling global impact by fostering a lymphoma ecosystem that ensures local change and evidence-based action.

Special Thanks

Special thanks to all patients and the LC member organisations who offered their insight and support as well as to the many other organisations, medical professionals and individuals who generously shared their knowledge, resources and understanding for this report.

Report Team

Natalie Dren, Shawn Sajkowski and Lorna Warwick.

Disclaimer

Lymphoma Coalition (LC) provides the 2019 Report Card on Lymphomas for general information related to topics relevant to lymphoma worldwide. While LC makes every effort to ensure accuracy, the information contained in the report is taken from various public and private sources. No responsibility can be assumed by LC for the accuracy or timeliness of this information.

Warning

LC's 2019 Report Card on Lymphomas should not be used for the purpose of self-diagnosis, self-treatment or as an alternative to medical care. If you have any concerns arising out of the information contained in this report, you should consult your own physician or medical advisor. If you suspect you have lymphoma, seek professional attention immediately.

Contents

Board of Directors

Susan Thornton | Chair
Cutaneous Lymphoma Foundation, USA

Rosmarie Pfau | Vice Chair
Lymphome.ch, Patientennetz Schweiz, Switzerland

Guy Bouguet | Treasurer
France Lymphome Espoir

Sarper Diler | Secretary
BirKan, Turkey

Monica Pasqualin | Director
ABRALE, Brazil

Lauren Pretorius | Director
Campaigning for Cancer, South Africa

Medical Advisory Board

Laurie H. Sehn, MD, MPH (LC Chair)
Chair, BC Cancer Lymphoma Tumour Group,
Clinical Professor, University of British Columbia,
Vancouver, British Columbia, Canada

Andreas Engert, MD
Professor, Internal Medicine, Hematology & Oncology,
University Hospital of Cologne,
Cologne, Germany

John G. Gribben, MD, DSc, FRCPath, FRCP, FMedSci
Professor, Consultant Haematologist
& Medical Oncologist,
Barts & The London NHS Trust,
London, England

Gilles Salles, MD
Professor of Medicine, University of Lyon,
Lyon, France

John Seymour, MD
Professor, Chair Department of Haematology
& Medical Oncology,
Peter MacCallum Cancer Centre,
East Melbourne, Australia

Julie Vose, MD
The Neumann M. and Mildred E. Harris
Professorial Chair,
Chief of Oncology/Hematology Division,
Department of Internal Medicine,
University of Nebraska Medical Center,
Omaha, Nebraska, USA

Message from the

Chair of the LC Medical Advisory Board

Laurie H. Sehn, MD, MPH
Chair, BC Cancer Lymphoma Tumour Group
Clinical Professor, University of British Columbia, Vancouver, Canada

The majority of patients diagnosed with lymphoma are over age 65 and the incidence rate of lymphoma in the older population is currently growing by 8-10% per year. Not only are incidence rates higher in those aged 65+, so are mortality rates. Worldwide population ageing means we will continue to see more and more older patients diagnosed with lymphoma.

Treating an older patient with lymphoma is complex. Older patients often have more comorbidities and may be frail, and as a result may not be able to tolerate the preferred treatment for their subtype compared to a younger, fit patient. **It is imperative a patient's biological age is determined before treatment, as treatment choice cannot be based on chronological age alone.** Some fit older patients can receive full-dose standard therapies that may be curative while frail patients should receive an adapted therapy that maintains quality of life.

Ideally, better treatment options are needed that increase survival with a low side effect burden and reduced toxicity. This report shows that while clinical trials investigating novel therapies in lymphoma are, for the most part, open to adult patients in all age groups (young, mid, old), the age-grouping proportions are not often disclosed and results relating to treatment response and adverse events are not stratified by age. Further, there are few clinical trials focusing specifically on the rapidly growing older population.

Within the research community, there is more we can do to address this need. Short-term, greater effort can be made to analyse clinical trials by age-grouping to increase understanding of who the ideal patient is to receive a new treatment. Long-term, let's develop more age-specific clinical trials that are representative of the subtype incidence rates.

Message from the

Chair of the
LC Board of Directors

Susan Thornton

CEO, Cutaneous Lymphoma Foundation

The LC Board of Directors and executive leadership recently updated the organisation's vision, mission and strategic plan. The new vision statement – equity in lymphoma outcomes across borders – reflects that patients have different needs, whether that is due to subtype of diagnosis, where they live, their age or any other qualifier. Equity means everyone should have the same opportunities to succeed despite these differences.

This Report Card emphasises the different factors influencing a recently diagnosed adult patient experience by age group (young, mid, old). What is clear is that patients in all age groups need more information and support beyond what is currently being provided, customised to their stage of life.

In each age group analysed, patients consistently reported doctors to be among their top three information sources. Patients are going to their doctors for information; however, as results throughout this report highlight, they are not always getting the answers or support they need—especially with emotional issues.

The proportion of patients using the internet for health research is also high. This is true even in the mid to old patient groups. There is a wealth of information available online, but it can be challenging for a patient to determine what is credible and applies to their particular lymphoma.

Patient organisations are not only a reliable source of information but also provide support to help cope with emotional concerns and other barriers to care. It's critical that patients know they are not alone, especially when they are less likely to discuss the psychosocial aspects of their disease with their doctors.

As a global coalition, we call for patients with lymphoma to be referred to patient organisations, ideally when diagnosed. Care and support of an individual extends beyond the clinic and can last for many years post-treatment.

Alongside healthcare professionals, patient organisations play an important role in helping ensure patients receive the right information and support they need to build their confidence, improve their overall experience and improve outcomes.

Message from the
Chief
Executive Officer

Lorna Warwick

The mission of the Lymphoma Coalition (LC) is enabling global impact by fostering a lymphoma ecosystem that ensures local change and evidence-based action. This requires all members of the lymphoma community to work together to positively impact patient care.

This *2019 Report Card on Lymphomas* highlights the different experiences of recently diagnosed patients with lymphoma and CLL, dependent on their age of diagnosis. Across all age groups, fatigue continues to be the top reported physical issue affecting well-being. Despite the massive impact of fatigue on health-related quality of life, the majority of patients are not referred onto appropriate fatigue-related information, support, or interventions. This needs to change, as there are steps patients can take to reduce their fatigue burden. Additionally, research into new therapies that do not exacerbate a primary symptom of lymphoma is needed.

This report also highlights that changes in relationships is the most prominent psychosocial issue, reported both during and after treatment across all three age groups. Patients must be prepared with information at the outset that acknowledges and normalises the possibility of this occurrence, as well as being directed to appropriate supports to help them navigate, adapt, and accept these changes may happen.

We ask that we all work to ensure that patients, upon diagnosis, are provided the proper pathway to credible information and support so they can go through their cancer experience with confidence.

Thank you for being part of the solution.

Many thanks to our financial supporters. It is through their support that we are able to undertake this important work that supports patients while, at the same time, identifies the gaps in patient care. Thank you as well to LC member organisations whose input has been most valuable.

Overview

Nearly every country in the world is experiencing growth in the number and proportion of older persons in their population.[1] Globally, the population aged 65 and over is the fastest growing age group; by 2050, one in six people in the world will be over 65.[1] Further, the number of persons aged 80 years and over is projected to triple, from 143 million in 2019, to 426 million in 2050.[1]

The demographic processes behind widespread population ageing include decreased fertility rates, reduced disease burden, and increased life expectancy.[1,2] The reduction in disease burden has been characterised by a shift from infectious and parasitic disease (tuberculosis, malaria, measles) to non-communicable and chronic conditions (cancer, heart disease, diabetes).[2]

Cancer is now among the leading causes of death worldwide[3], and the number of cancer patients and survivors is increasing.[4] There is a higher incidence of cancer with ageing; cancer often occurs in persons of older age (65+), and older patients with cancer constitute the largest and fastest growing group of cancer patients.[4,5] There is also higher mortality among older patients with cancer.[3,6]

As this pertains to lymphomas, over the past two decades, the incidence of lymphoma has stabilised in younger patients but has increased by 8-10% per year in the elderly.[7] The median age of diagnosis (excluding Hodgkin lymphoma cases) is 67 years, with most patients being diagnosed between the ages of 65-74 (figure 1).[3] The median age at death (excluding Hodgkin lymphoma cases) is 76 years, with the highest percentage of deaths occurring among patients 75-84 years old (figure 2).[3]

Figure 1. Percent of new lymphoma cases (excluding Hodgkin lymphoma) by age group.
SEER 21 2012-2016. US only, all races, both sexes.[3]
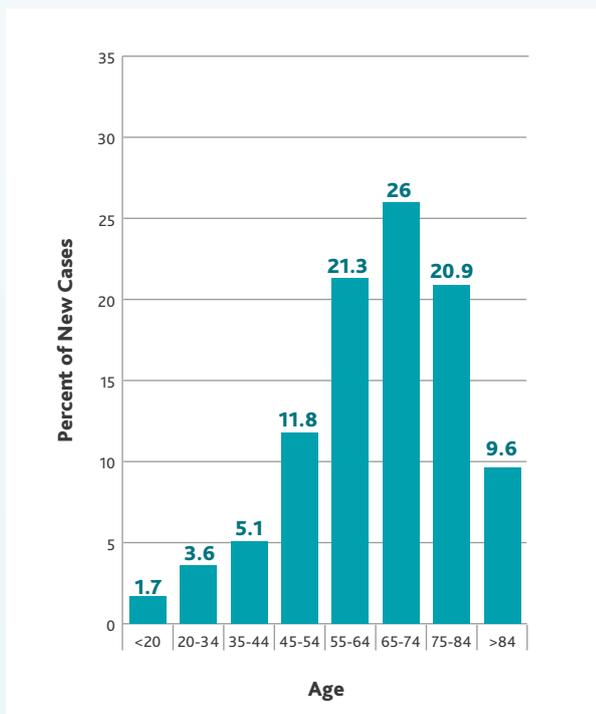
Figure 2. Percent of lymphoma-related deaths (excluding Hodgkin lymphoma) by age group.
SEER 21 2012-2016. US only, all races, both sexes.[3]
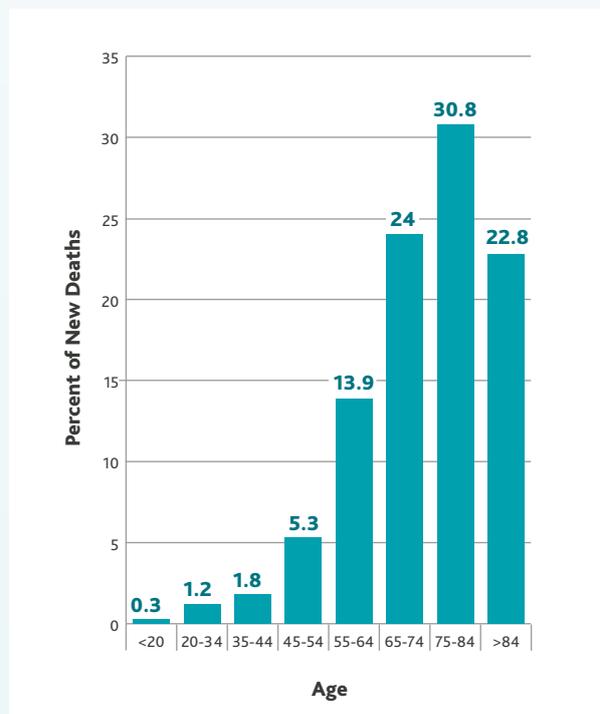
Despite the growing population of older cancer patients, there are a limited number of research projects and initiatives that focus on the experience of these patients.[4] Further, cancer as experienced by different patient age groups has not been well-studied generally.

As such, Lymphoma Coalition (LC) saw the need in the *2019 Report Card on Lymphomas* to examine the age-related lymphoma patient experience.

Using a subset of data from the LC 2018 Global Patient Survey on Lymphomas and CLL (LC 2018 GPS), this report will specifically examine the experiences of lymphoma patients within the following age categories:

1. Young (18-59) (n=1473)

2. Mid (60-69) (n=371)

3. Old (70+) (n=162)

This report focuses on newly diagnosed patients and those within their first year of being diagnosed with lymphoma. The *2018 Report Card on Lymphomas* highlighted that patients face a multitude of concerns and uncertainties during this timeframe as they adapt to their diagnosis and initial care. It is relevant and important to identify areas where patients require additional information and support during this time.

Within each of these age-groupings, key patient-reported issues have been highlighted, including:

- **Informational needs and understanding levels**
- **Physical conditions and medical issues**
- **Psychosocial issues**
- **Patient-doctor communication**
- **Barriers to treatment (including therapy and clinical trial access)**

Methodology

The information in this report is largely based on the learnings from the 2018 Lymphoma Coalition Global Patient Survey on Lymphomas and CLL (LC 2018 GPS). Globally, there were 6,631 respondents from 70+ countries. There were 2,006 participants included in this sub-analysis.

The LC 2018 GPS did not ask age of diagnosis, rather current age and year diagnosed. Therefore, for accuracy, only patients who indicated being diagnosed in 2017 were included in the analysis. The GPS ran from January to March of 2018, so if patients were diagnosed in 2017 (2018 was not an option), they would still be their indicated age or very close to (one year older if birthday was January-March) and fit the criteria of being within one year of diagnosis.

This methodology ensured that patient experience was reflective of current age and excluded cases where patients had been diagnosed and treated many years ago (i.e. person who was currently 65 but was diagnosed/treated and had their patient experience when they were 20).

A full demographic comparison of the three age groups was completed (Appendix A). The age groups were similar on many analysis points (gender, education level, area of residence); however, differed in their main lymphoma subtypes. The top three subtypes reported by age group are shown in table 1.

Table 1. Top three subtypes reported by age group

Young	Mid	Old
Hodgkin 22%	DLBCL (unspecified) 17%	DLBCL (unspecified) 22%
Follicular 13%	CLL/SLL* 11%	WM* 18%
DLBCL* (unspecified) 13%	Follicular 11%	Mantle cell 14%

*DLBCL- diffuse large B-cell lymphoma, CLL/SLL- chronic lymphocytic leukaemia/small lymphocytic lymphoma, WM-Waldenstrom's macroglobulinaemia

Additionally, patients from China comprised a large proportion of each age group (young 60%, mid 54%, old 40%). It must be noted that this may exert some level of influence on the patient experience data. To account for this, a comparison was completed excluding patients from China and any major differences are highlighted within the text. Data from the LC 2018 GPS was supplemented with information from scientific peer-reviewed journals, clinical trial databases, and drug regulatory and reimbursement websites.

Objectives

- **Identify key issues and challenges in each patient age-grouping**
- **Identify issues that are consistent across age-groupings**
- **Determine specific areas where patients require additional information and support**

Informational Needs and Understanding Levels

Patients who have been newly diagnosed with lymphoma face many uncertainties and have many questions and concerns. The LC 2018 GPS indicated the majority of all three patient groups (young, mid, old) wanted additional medical and/or support information beyond what was provided at their diagnosis meeting with the doctor (table 2). The greatest need for information was observed in the young patient group (73%) (table 2). When patients from China were excluded from this analysis, informational needs slightly decreased.

Table 2. Did patients want additional medical and/or support information at their initial diagnosis meeting?

	Young (%)	Mid (%)	Old (%)
Yes*	73	63	55
No	4	6	4
No because I received enough information	14	19	33
Did not want more information at the time, too overwhelmed	9	12	8
Total	**100**	**100**	**100**

*Those who reported 'yes' excluding patients from China: young 57%, mid 46%, old 40%.
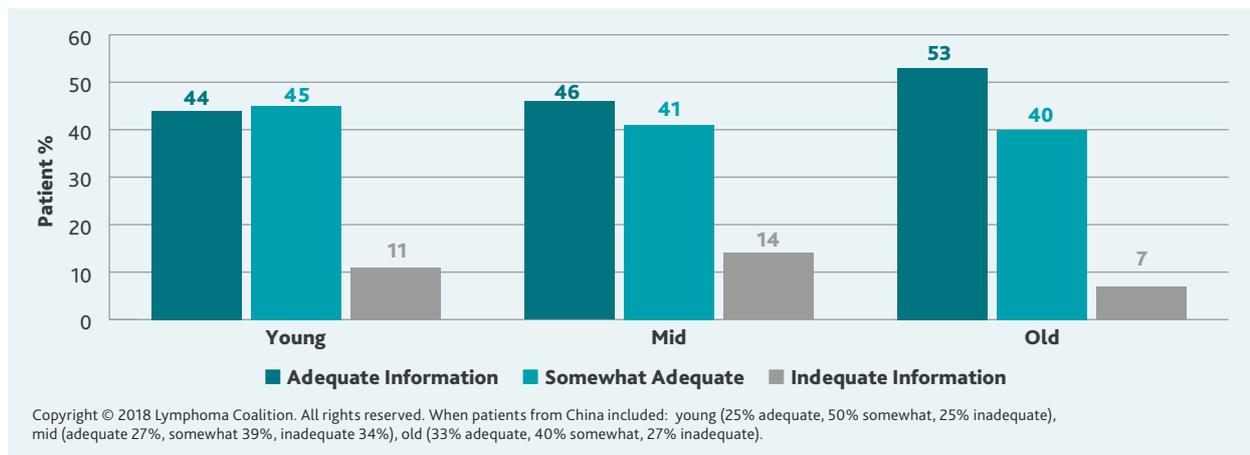
Given this need for more information, it is unsurprising that many patients are leaving their initial diagnosis meeting with insufficient understanding of their diagnosis and care plan. Across all three age groups, less than 40% of patients indicated having a very good (level 5) understanding of their treatment options, stages of care or side effect management. Overall, slightly more patients understood their actual diagnosis.

It was also observed that the highest proportion of poor understanding (level 1) was reported by the mid-age group in all categories (mid and young when China excluded from analysis), and the highest proportion of very good understanding (level 5) was reported by the old age group in most categories. The majority of patients in all three age groups reported seeking additional information immediately following their diagnosis, and 1-3 months following diagnosis.

Less than 55% of patients across all three age groups reported having adequate information (figure 3). As was noted earlier, informational needs decrease when China is excluded from the analysis, therefore figure 3 summarises data excluding China to improve accuracy and reduce confounders. The largest proportion of inadequately informed patients was observed in the mid age group (14%) and the largest proportion of adequately informed patients was observed in the old age group (53%).

All three age groups reported using the same top three information sources: doctors, websites, and patient organisations (figure 4). While the proportion of patients going to their doctor for information is high (young 63%, mid 62%, old 67%), so is the proportion of patients using the internet (young 64%, mid 55%, old 50%). When patients from China were excluded in this analysis, it was found that the young group also highly reported using online blogs for information (44%).

Figure 3. Level of information patients felt they had overall (excluding patients from China)

Chart data:
- Young: Adequate Information 44, Somewhat Adequate 45, Indequate Information 11
- Mid: Adequate Information 46, Somewhat Adequate 41, Indequate Information 14
- Old: Adequate Information 53, Somewhat Adequate 40, Indequate Information 7

Legend: Adequate Information, Somewhat Adequate, Indequate Information

Y-axis: Patient %

Figure 4. Patient's top three information sources

Chart data:
- Young: Doctor 63, Websites 64, Patient Organisations 45
- Mid: Doctor 62, Websites 55, Patient Organisations 42
- Old: Doctor 67, Websites 50, Patient Organisations 39

Legend: Doctor, Websites, Patient Organisations

Y-axis: Patient %
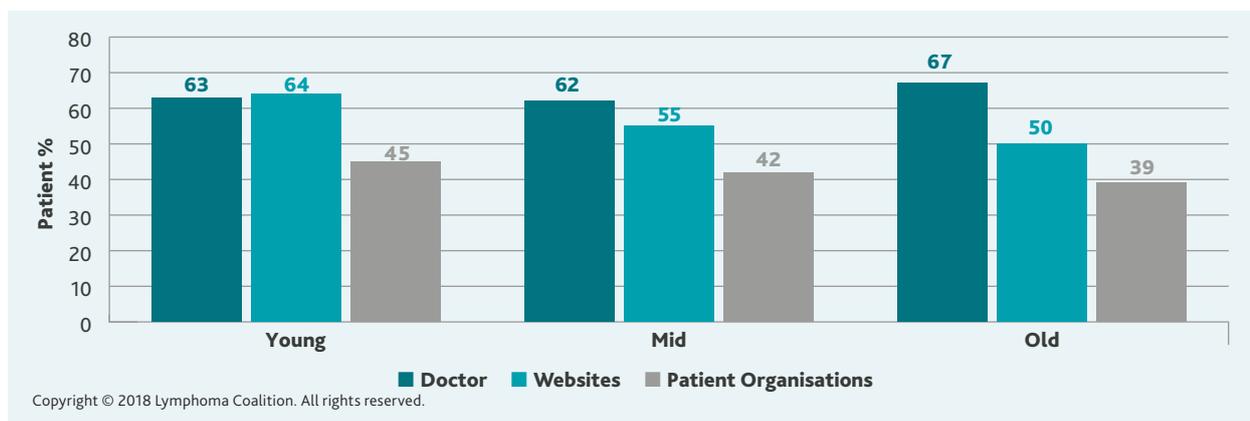
There is some doubt surrounding the idea that older patients use the internet for health research. However, recent studies suggest that for many older adults, besides their healthcare provider, the internet is one of the first preferred information sources.[5,8] European statistics (Eurostat) on internet activities (in the past 3 months) by age group show that 60% of those aged 59-74 use the internet to seek health information.[9] This was a greater percentage than what was observed in the 16-24 year old age group (48%).[9]

Unfortunately, many older patients experience difficulty using online health information.[5] Studies have found that older adults report experiencing challenges in navigating the internet and identifying accurate and reliable online health information sources.[10] Additionally, studies suggest that older adults have a greater amount of trust in a person with whom they are able to actively discuss their health (i.e. doctor) as opposed to a non-living source (i.e. the internet) which they have to access or manipulate.[10]

Like every other age group, older adults are a diverse group and their internet capabilities and activities are diverse.[8] As such, older adults have varying needs regarding how information should be presented. Studies suggest that mode tailoring might be a promising strategy to optimise online health information for the older population.[5] Mode tailoring allows individuals to adapt how online information is presented according to their preferences, using text, visual, and audio visual information.[5] Because mode tailoring requires some basic internet competencies, some less technological suggestions include modifying website font (size, type), readability, and navigation in order to accommodate an older audience.[10]

Patient Experience

Physical Conditions and Medical Issues

*No significant differences observed in this section relating to patients from China being included or excluded in data analysis.

Since this patient pool only includes those who were diagnosed in 2017, the majority of patients in each age group reported being in active treatment. The top three stages reported by age group were:

6%		
16%		
57%		
Young		

Legend: ■ First line treatment ■ Maintenance therapy ■ Watch and wait

Young: 6%, 16%, 57%
Mid: 16%, 11%, 53%
Old: 14%, 17%, 57%
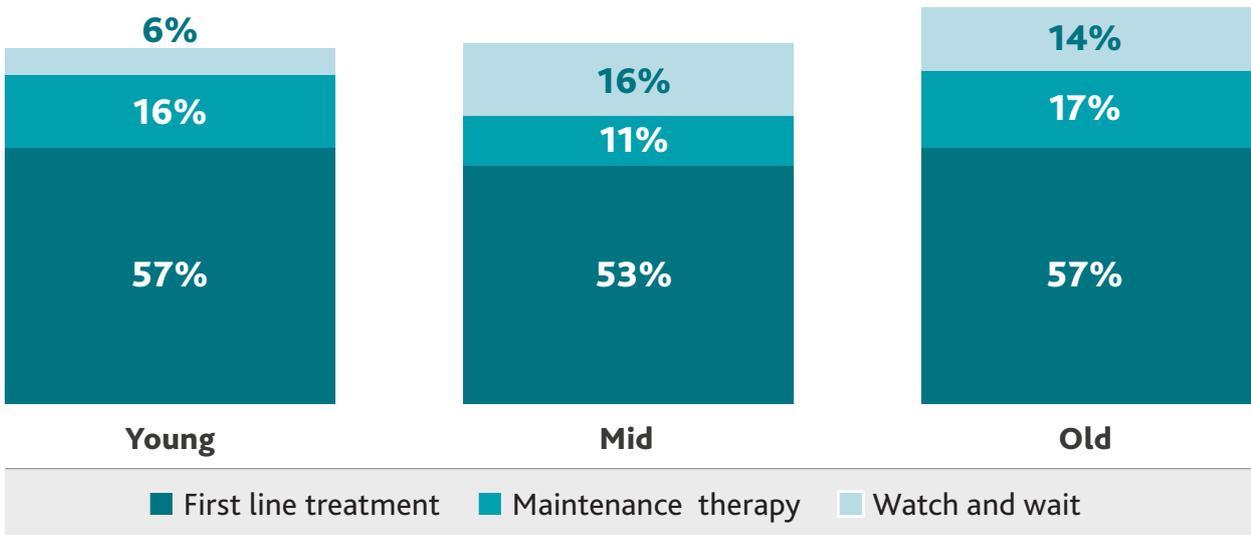
Across the three age groups, the top reported physical conditions and medical issues were commonly reported treatment side effects, reflecting the large proportion of patients who were in treatment (table 3).

Table 3: Top three physical conditions reported by age group

Young	Mid	Old
Fatigue 67%	Fatigue 69%	Fatigue 62%
Hair loss 54%	Changes in sleep patterns 40%	Muscle weakness 40%
Changes in sleep patterns 42%	Muscle weakness 36%	Hair loss 36%

Across all three age groups, **fatigue** was the top reported physical condition affecting well-being. Patients were asked to indicate if they had experienced changes in various areas of life as a result of their fatigue (figure 5).

Figure 5. Areas of life affected by fatigue
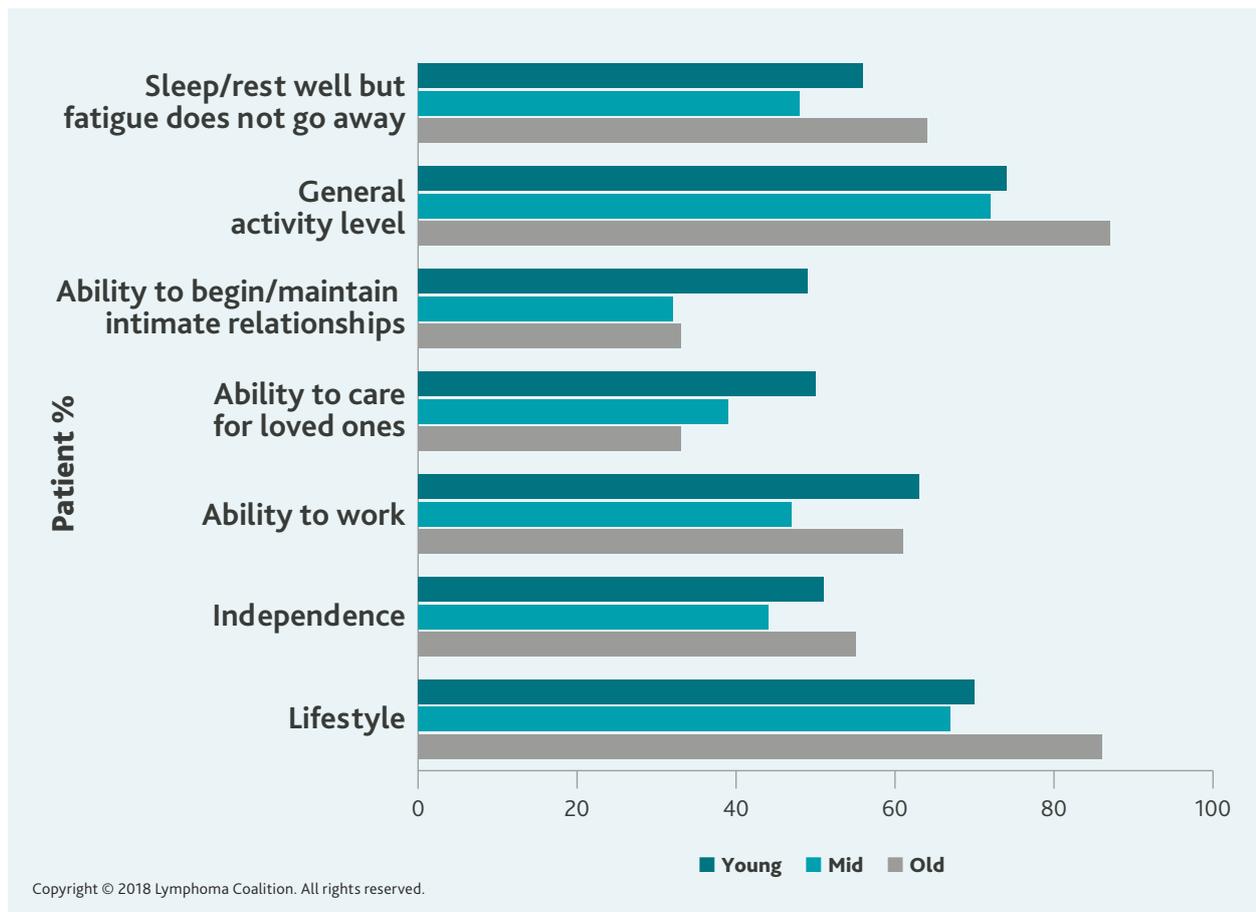
While lifestyle and general activity level were top reported affected areas by all three groups, there were also some age group specific trends. For example, compared to the young and mid groups, a greater proportion of those in the old group reported that their lifestyle (86%) and general activity level (87%) had been affected. The young group reported that fatigue particularly affected their ability to work (63%), their ability to care for loved ones (50%), and their ability to begin and maintain intimate relationships (49%). The mid age group reported the least amount of life changes in the majority of categories.

The top 3 medical issues (during and after treatment) reported by age group are described in figure 6.

Figure 6. Top three medical issues reported by patients during and after treatment according to age group; (a) young, (b) mid and (c) old

(A) Young

Patient %

During treatment:
- Neutropenia: 56
- Stomach-related Issues: 48
- Pain: 35

After treatment:
- Neutropenia: 40
- Stomach-related issues: 30
- Issues with other organs: 28

■ During treatment ■ After treatment

(B) Mid

Patient %

During treatment:
- Neutropenia: 56
- Stomach-related issues: 41
- Issues with other organs: 30

After treatment:
- Neutropenia: 40
- Stomach-related issues: 22
- Osteoperosis: 22

■ During treatment ■ After treatment

(C) Old

Patient %

During treatment:
- Neutropenia: 49
- Pain: 30
- Numbness: 28

After treatment:
- Neutropenia: 28
- Diarrhoea: 22
- Any other blood condition: 22

■ During treatment ■ After treatment

The age groups shared many of the same top three medical issues; however, while the young and mid groups reported stomach-related issues both during and after treatment, the old group did not report this as a top issue at either time point.

Additionally, in the majority of cases, the reported prevalence of each medical issue was highest in the young group and lowest in the old group—with the mid group prevalence falling in between. This was true both during and after treatment.

Studies with similar findings suggest this could relate to the fact that younger patients are often receiving more aggressive and toxic therapies than older patients, leading to more and harsher side effects.[11] Older patients might also be more reluctant to report medical issues because they fear additional testing and treatments and view their health problems as a normal part of ageing.[4]

Psychosocial Issues

Studies examining the impact of ageing on the psychosocial experiences of cancer patients have produced inconsistent results. Some studies suggest older patients become increasingly vulnerable to psychosocial distress as their social and financial resources begin to diminish, and they experience accumulating personal and health-related losses.[4] However, there are also many studies suggesting that younger patients with cancer report more psychosocial issues than older adult patients.[4,11] The LC 2018 GPS results were consistent with the latter.
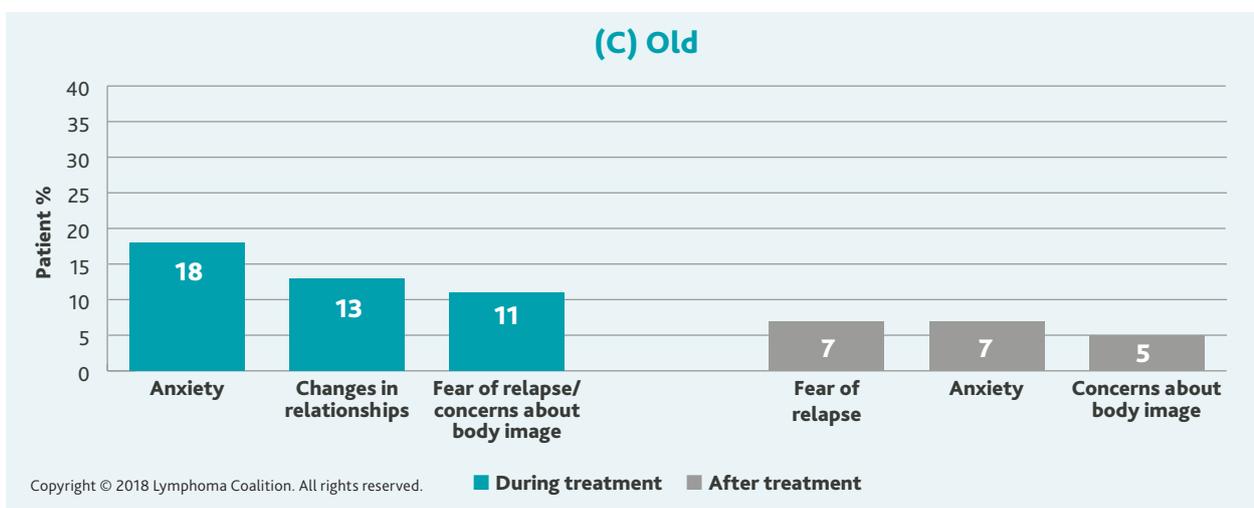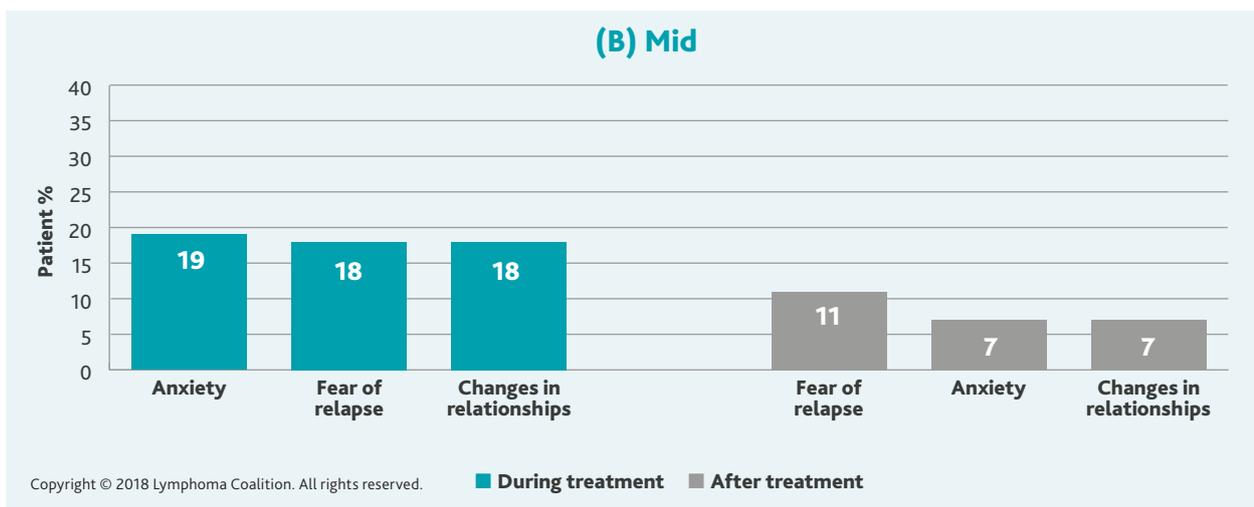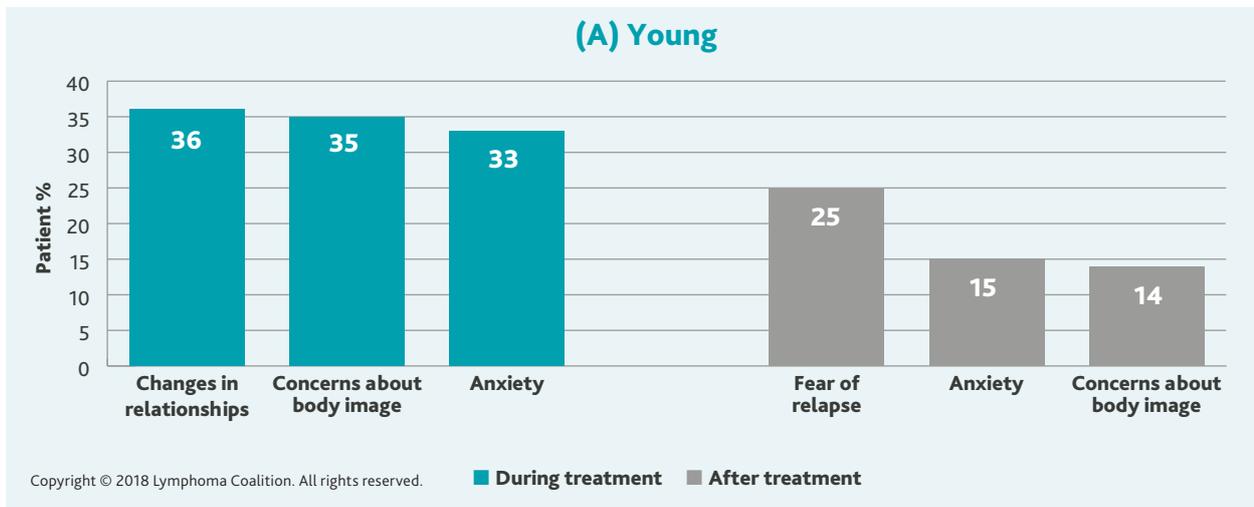
Compared to the mid and old patient groups, a larger proportion of the young patient group reported that their lifestyle (86%; compared to 70% & 67% respectively) and independence (61%; compared to 49% & 46% respectively) had been affected because of their lymphoma.

This may reflect the fact that patients in the young group would likely still be working, living independently, raising families and sustaining high levels of activity. Patients in the mid and old groups may already be retired, dealing with reduced mobility, lower activity levels, and some losses of independence.

Additionally, both during and after treatment, the reported prevalence of each psychosocial issue examined was highest in the young group and lowest in the old group. The mid group prevalence often fell between the young and old groups. While this trend was true both including and excluding patients from China in the analysis, the top three psychosocial issues reported (during and after treatment) differed significantly depending on whether or not China was included.

When patients from China were included, financial issues were a top reported concern for all three age groups both during and after treatment. China's 'out of pocket' system for healthcare creates high stress and has a large financial impact for patients; many middle class households in Asia face impoverishment after paying for cancer care. This is not the case in all countries, therefore, for accuracy, the percentages reported in figure 7 below (top psychosocial issues during and after treatment) reflect data excluding patients from China.

Figure 7. Top three psychosocial issues reported by patients (excluding patients from China) during and after treatment according to age group; (a) young, (b) mid and (c) old

(A) Young

Patient %

During treatment			After treatment		
Changes in relationships: 36	Concerns about body image: 35	Anxiety: 33	Fear of relapse: 25	Anxiety: 15	Concerns about body image: 14

■ During treatment   ■ After treatment

(B) Mid

Patient %

During treatment			After treatment		
Anxiety: 19	Fear of relapse: 18	Changes in relationships: 18	Fear of relapse: 11	Anxiety: 7	Changes in relationships: 7

■ During treatment   ■ After treatment

(C) Old

Patient %

During treatment			After treatment		
Anxiety: 18	Changes in relationships: 13	Fear of relapse/ concerns about body image: 11	Fear of relapse: 7	Anxiety: 7	Concerns about body image: 5

■ During treatment   ■ After treatment

Some studies suggest that while different age groups may be facing similar patient experience-related psychosocial issues (i.e. changes in relationships, anxiety, depression, stress related to finances), older patients often have more overall life stability, or have developed coping mechanisms that lessen the severity of the impact of these issues.[4,11] Alternatively, some studies indicate there may be some underreporting of psychosocial issues among older patients, as the measurement tools used to assess these issues are not always adjusted for older persons.[4] For example, identifying depression in older adults requires a different approach than what is used for younger adults. This is because older persons are often less likely to disclose affective symptoms like sadness, and instead present with more physical symptoms like trouble concentrating and fatigue.[4]

Changes in relationships and anxiety were top reported issues both during and after treatment across all three age groups. These issues likely have different causes and manifestations as they pertain to the different age groups. For example, younger patients often report feeling as though they are living in a different world from the world they previously shared with others. They are likely navigating changes in romantic, workplace and social relationships, and they may find themselves having to fill a new role in their family.[12] They may be facing financial pressures stemming from loss of employment, working reduced hours, and having to continue to support a family.[12] Concerns about body image, which was a top reported concern for young patients both during and after treatment, could also be contributing to their anxiety and changing relationships.

Mid to older patients may face many similar changes in relationships but may also be facing greater losses of independence, for example needing a caretaker or being moved to an assisted living facility. All of these factors could be anxiety-causing. They also experience financial pressures relating to declining financial resources, fixed incomes, and increasing costs relating to healthcare and caretaking.
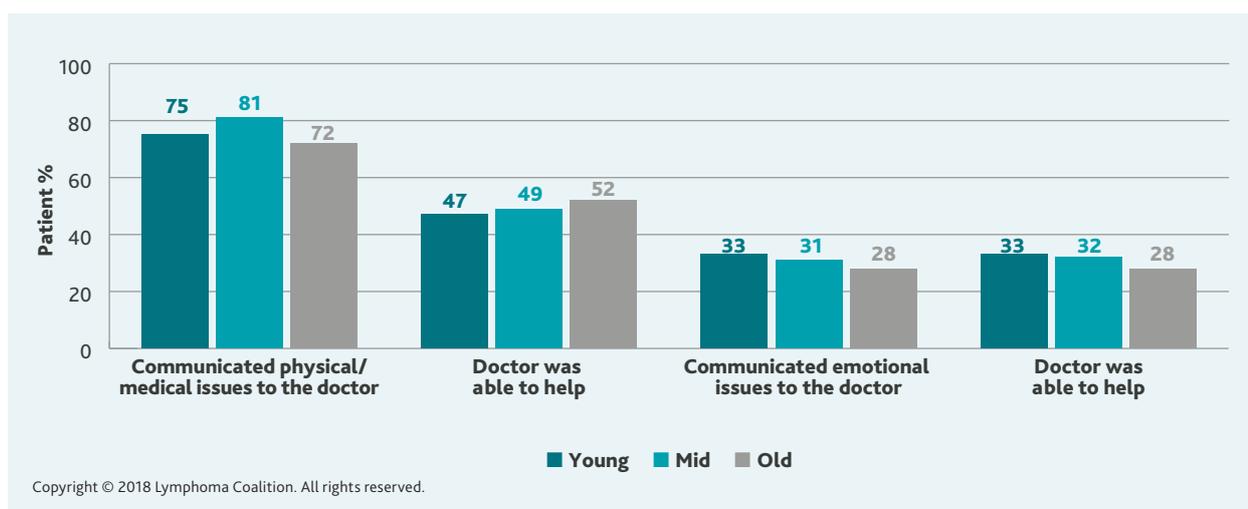
Life-stage should be a consideration as support systems are established to help patients cope.

Fear of relapse was the top reported psychosocial issue following treatment for patients in all three age groups. When treatment ends, patients lose the support provided by regular contact with oncology staff, and so experiencing some emotional upheaval is common. **As this is when fear of relapse is most expected and observed, it is critical for it to be recognised, openly discussed, and met with appropriate intervention and support.** This is important because across comorbidity studies, fear of relapse is consistently reported to be a predictor of overall quality of life, mental health-related quality of life, and physical health-related quality of life.

Patient-Doctor Communication

Across all three age groups, a greater proportion of patients reported communicating physical/medical issues to their doctor than emotional issues (figure 8). Additionally, across all three groups, more patients reported that the doctor was able to help with medical issues than with emotional issues. Less than 35% of patients in all age groups felt helped with their emotional issues.

Figure 8. Patient-doctor communication by age group

Copyright © 2018 Lymphoma Coalition. All rights reserved.

Despite high patient reports of discussions about physical/medical issues with their doctor, patients in all age groups were not being adequately supported with their top reported physical issue affecting wellbeing - fatigue.

Fatigue was the top reported physical condition in every age group; however, only **38%** of those in the young group, **34%** in the mid group, and **31%** in the old group were referred onto further support for their fatigue.

Relating to support with emotional issues, fear of relapse was the top reported psychosocial issue following treatment for patients in all three age groups. Of those who discussed their fear of relapse with their doctor (young 42%, mid 32%, old 21%), only 30% of young patients, 28% of mid-age patients, and 25% of old patients felt their discussion helped alleviate the fear. The same trend was apparent in a sub-analysis that excluded patients from China, but with a lower percentage of patients across all three groups discussing their fear with their doctor (young 36%, mid 25%, old 17%). Further, across all three age groups, less than 40% of those who discussed their fear of relapse with their doctor were referred onto further support (young 38%, mid 35%, old 30%).

Studies suggest that older patients are most at risk for poor communication with healthcare providers because of age-related declines, for example in cognitive (i.e. memory) and physical (i.e. vision loss, hearing loss) functioning.[5]

Older patients are often less likely to express their information needs or preferences and participate less actively during consultations.[5] Further, older patients can experience lower self-efficacy in obtaining relevant information from their doctor, and have more difficulty remembering and using this information.[5] This translated in the LC 2018 GPS data in terms of discussing and receiving support for side effects. While the proportion of patients who discussed and received help with side effects was relatively high across the three age groups (figure 9), the lowest proportion in each category was observed in the old patient group. When a sub-analysis was performed excluding patients from China, these percentages dropped even further for the old group (52% asked questions about side effects, 49% had their questions answered by their doctor, 40% were helped with coping with side effects).

Figure 9. Patient-doctor communication by age group
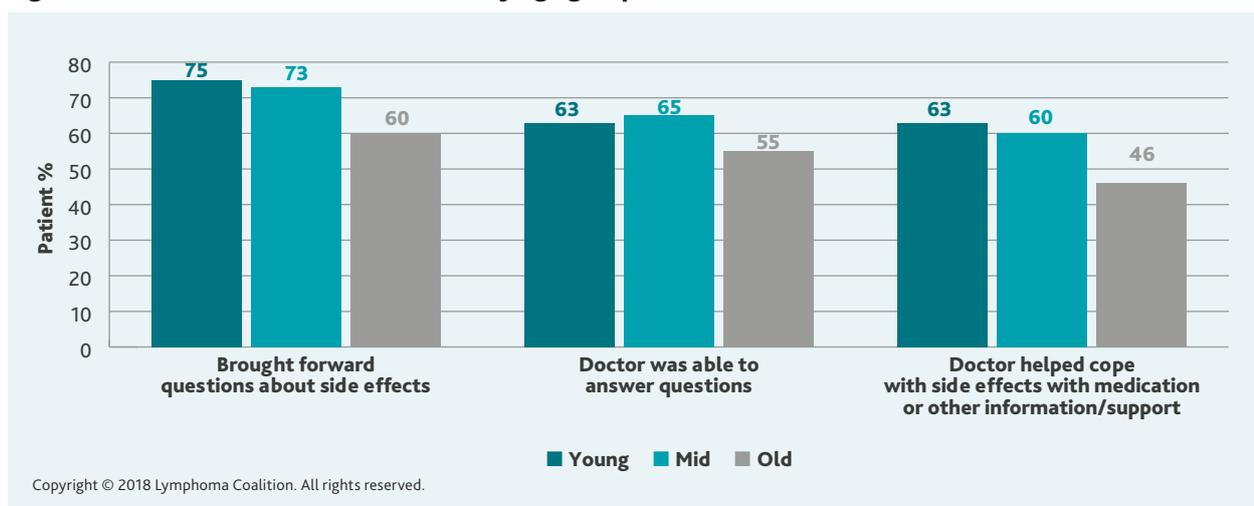
Older patients could benefit from additional support from healthcare providers, and/or referrals onto necessary supportive care and services. It is also advised that a caregiver, or a family member or friend be present during important conversations with healthcare providers. They can help ask questions, record the answers, and will also provide support during the discussion.

Therapy and Clinical Trial Analysis

Over the past two decades, advances in research and technology have led to the development of many new lymphoma therapies that are improving health outcomes for patients. However, the processes by which these new therapies are developed and approved for use are not always the most representative of the cancer population at large. Despite the fact that older patients comprise a significant portion of the patients seen in clinical practice, there is a lack of representation of older patients in clinical trials.[13]

Given that older patients with cancer constitute the largest and fastest growing group of cancer patients, it is imperative that greater attention be directed towards this demographic in therapeutic development.

It is expected that over the next few years, there may be a shift in treatment of elderly patients towards more intensified therapies with a curative intent.[7] Effective therapy options for older patients with aggressive lymphomas are needed because this patient population is growing. Selecting optimal treatments for older patients with aggressive lymphomas is difficult, and the outcomes for these patients can be worse due to comorbidities, decreased organ function and other factors.[7] As such, older patients (especially those 80+ years) are not typically given standard therapies, or standard therapy doses under the assumption that they cannot tolerate it. While this is certainly true for some patients, there is a need to identify 'fit' older patients with aggressive lymphomas to receive full standard dose at first-line.[6] Evidence already exists supporting the use of more aggressive therapies in older patient populations in various lymphoma subtypes including diffuse large B-cell lymphoma (R-CHOP standard[14], CAR-T[15]), and mantle cell lymphoma (cytarabine-based induction/ASCT[16]) among others.

For this shift in treatment to happen, fit older patients must be identified using frailty (i.e. CIRS-G) and comorbidity (i.e. G8) assessments, and older patients must be sufficiently represented in clinical trials. The evidence underpinning many currently approved lymphoma therapies is derived from younger and risk-favourable cohorts, which do not reflect the real-world lymphoma population (median age of diagnosis 67[3]).[16]

Therapy Analysis

The LC conducted a therapy analysis to gain an understanding of the age representation in some recently approved lymphoma therapies. Therapies selected for analysis were determined by 'novel' therapies approved in the European Union for five lymphoma subtypes (chronic lymphocytic leukaemia, follicular, diffuse large B-cell, mantle cell, Waldenstrom's macroglobulinaemia). These were the top five subtypes represented in the mid and old age-groupings in the LC 2018 GPS. 'Novel' is defined as therapies approved within the last five years. All of these therapies are also approved for use in the USA. Clinical data for selected therapies was gathered from the European Medicine Agency's (EMA) European Public Assessment Reports (EPARs) which are used as clinical evidence in the approval decisions issued by the European Commission. Please see Appendix B for detailed results.

It was determined that approvals of each of these therapies were based on clinical trials that were open not only to the young group, but also to the mid to old age-groupings (60+) (Appendix B). The mean age of trial participants was not widely available; however, median ages were often disclosed and ranged from 56-73 years old. Where age-grouping proportions were available, the proportion of trial participants aged 65 and older ranged from 24% to 64%. One clinical trial (obinutuzumab+ chlorambucil for CLL first-line) reported that 44% of patients were over the age of 75.

This analysis noted a major limitation of the clinical trial data used in these therapy approvals; none of the trial results relating to treatment response or adverse event data were stratified by age (Appendix B).

Therefore, even if a clinical trial has a representative population, it cannot be determined from the information available what age groups had the worst/best response or the most/least adverse events. This has implications for the effectiveness of a therapy in an older patient population if, for example, the positive results were mostly noted in the younger, more risk-reduced portion of the clinical trial population or vice versa.

Clinical Trial Analysis

Beyond recently approved therapies, the LC also conducted a wider age-related analysis of active phase II and phase III interventional studies involving novel agents and new or existing therapy combinations. This analysis focused on the same five lymphoma subtypes that were included in the therapy analysis (chronic lymphocytic leukaemia, follicular, diffuse large B-cell, mantle cell, Waldenstrom's macroglobulinaemia). Clinical trial data was gathered from internationally recognised clinical trial databases including Clinicaltrials.gov, EU Clinical Trials Register, World Health Organization, Cancer Trials Australia, and the Netherlands Trial Register. Please see Appendix C for detailed results.

Novel therapy clinical trial eligibility for each subtype was examined by age requirement parameters; specifically, by young (18-59), mid (60-69), and old (70+) age-groupings (Appendix C). Across all subtypes, the age requirements for trial participation were not particularly exclusionary of any of the age groups. Out of all novel therapy trials analysed (n= 951), only 26 had an age cut off of 60 (exclusion of patients over 60), 27 had an age cut off of 75, and 18 had an age cut off of 80. Additionally, there were 70 CAR-T therapy trials included in the analysis, 46 of which were eligible to patients 70 years and older (29 outside of China). The young group was eligible for the most novel clinical trials, ranging from 97-100% across subtypes. The mid group was eligible for 82-92% across subtypes, and the old group was eligible for 75-83% across subtypes, given they meet other trial inclusion criteria. Though the mid to older patient groups were not overly restricted from clinical trial participation, this is not to say that these populations were sufficiently represented in any of these trials—this data was not analysed.

What this analysis did highlight was a lack of clinical trials focused specifically on developing novel therapies for older patients. Across all subtypes, there were only 15 novel therapy clinical trials limited to the mid and old groups (60-69, 70+), and only six trials limited to the old group (70+). The population of older patients with lymphomas is growing, and effective therapeutic options are needed—especially therapies for aggressive lymphomas and therapies with curative intent.[7]

A specific avenue requiring attention is the development of novel therapies specifically for the older lymphoma population, taking into account known risk-factors, comorbidities, and more relevant trial end points beyond overall survival (i.e. quality of life, toxicity, functional independence).

Barriers in Receiving Lymphoma Treatment

The LC also used the 2018 GPS data to examine the barriers that patients currently face in receiving their lymphoma treatments. The three age groups reported the same top three barriers: financial, wait time to treatment that was longer than necessary, and access to the most up to date treatment (figure 10).

While most barriers were reported at similar levels across the age groups, the young group was disproportionally affected by financial barriers (32%).

Patients in the young group would likely still be employed and/or raising families, so it makes sense that they may feel loss of income (i.e. having to stop working or working reduced hours) and the expenses related to care more.

Figure 10. Top three barriers in receiving lymphoma treatment
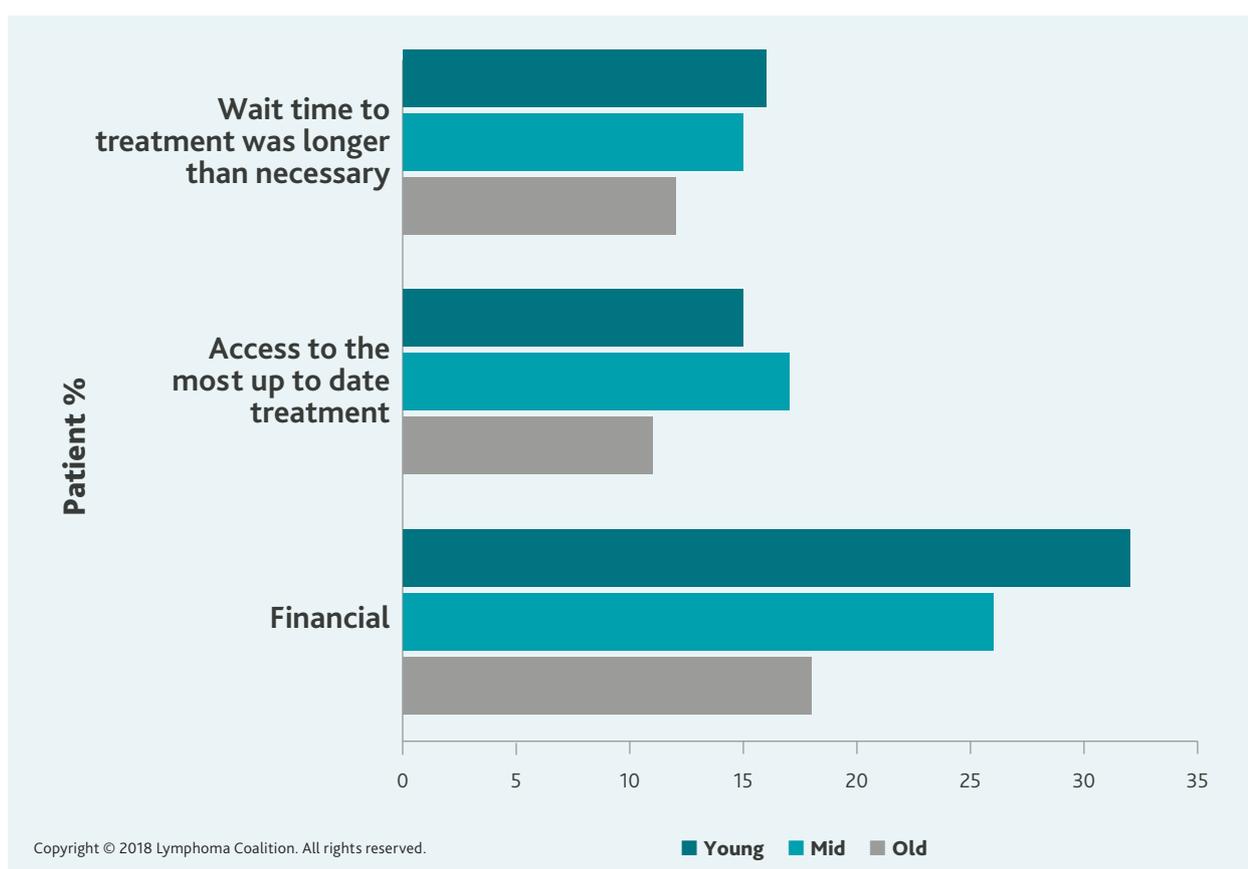
In addition, access to a treatment centre or prohibitive travel was a leading concern for the young and old in a sub-analysis that excluded patients from China, as was the availability of a specialty physician for the mid and old age groups.

Moving Forward

This *2019 Report Card on Lymphomas* emphasises that patients in all age groups need more information and support beyond what is currently being provided. While certain age-specific trends were identified, the majority of patient-reported issues span across all three of the age groups examined.

- After the initial visit with the doctor, **greater efforts are needed to ensure that patients have a thorough understanding** of their diagnosis, their treatment options and stages of care, and potential side effects as well as how they will be managed.

- In each age group analysed, patients consistently reported doctors to be among their top three information sources. Patients are going to their doctors for information; however, as results throughout this report highlighted, they are not always getting the answers or support they need—especially with emotional issues. Less than 35% of patients in all age groups felt helped by their doctor with emotional issues. **Doctors cannot be expected to provide all the support and information patients require, but it is critical that patients be referred onto other resources such as local patient organisations or psychological interventions/care.**

- While the proportion of patients going to their doctor for information is high, so is the proportion of patients using the internet for health research. This is true even in the mid to old patient groups. **It is important to take into account older adults have varying needs regarding how online information should be presented**; mode tailoring might be a promising strategy to optimise online health information for the older population. Some less technological suggestions include modifying website font (size, type), readability, and navigation.

- The most prominent physical condition affecting well-being, being top reported in all age groups, was fatigue. Despite the massive impact of fatigue on health-related quality of life, the majority of patients in all age groups who experienced fatigue were not referred onto further support by their doctor. **Patients need to be referred onto appropriate fatigue-related information, support, and interventions.** Additionally, research into new therapies that do not exacerbate a primary symptom of lymphoma is needed.

- The most prominent psychosocial issue, being top reported both during and after treatment across all three age groups, was changes in relationships. Patients must be prepared with information at the outset that acknowledges and normalises the possibility of this. **Patients must also be directed to appropriate supports to help them navigate, adapt to, and accept these changing relationships.**

- Compared to the mid and older patient groups, the **young patient group is disproportionality affected by both physical/medical and psychosocial issues.** This likely owes to their more intensive treatment regimens and their engaged life-stage (employment, raising families, and social activities) which can feel a more severe impact of a cancer diagnosis/treatment. This leads to the need for better treatment options with less toxic side effect profiles. Additionally, patients in this group must be screened for and directed towards information and support for their psychosocial issues (especially pertaining to financial burden).

- While clinical trials investigating novel therapies in lymphoma are, for the most part, open to patients in all three age groups (young, mid, old), their age-grouping proportions are not often disclosed, and their results relating to treatment response and adverse events are not stratified by age. Further, there are few clinical trials focusing specifically on the older patient population which is rapidly growing. **Developing age-specific clinical trials and novel therapies, as well as making greater efforts to analyse clinical trials by age-groupings are two important calls to action.**

Appendix A: Age Group Demographics

Sex	Young Group (18-59) n=1473	Mid Group (60-69) n=371	Old Group (+70) n=162
	Young (%)	Mid (%)	Old (%)
Male	48	56	57
Female	52	44	43
Totals	**100**	**100**	**100**

Subtype	Young (%)	Mid (%)	Old (%)
CLL/SLL	5	11	7
Burkitt	1	0	0
DLBCL (unspecified)	13	17	22
DLBCL GCB	6	4	6
DLBCL ABC	11	8	7
Follicular	14	11	4
Hodgkin	22	4	3
MALT/MZ	3	3	1
Mantle Cell	3	9	14
Peripheral T-cell	3	6	3
Anaplastic Large Cell	2	1	0
Extranodal Killer T-cell	5	2	0
Cutaneous	2	3	4
Transformed	0	1	0
WM	2	14	18
Other Indolent lymphomas	2	2	2
Other Aggressive lymphomas	3	1	3
Don't Know	3	3	6
Totals	**100**	**100**	**100**

Area	Young (%)	Mid (%)	Old (%)
Rural	26	24	16
Suburban	17	25	38
Urban	57	51	46
Totals	**100**	**100**	**100**

Education	Young (%)	Mid (%)	Old (%)
No schooling completed	2	9	7
Pre-secondary school	2	4	6
Some secondary school, no diploma	10	16	9
Secondary school diploma or equivalent	23	27	20
Some college/university, no diploma/degree	11	5	10
College/university diploma/degree	36	21	27
Trade/technical/vocational training	3	2	2
Master's degree	8	10	7
Doctorate degree	1	2	4
Professional degree	3	4	8
Total	**100**	**100**	**100**

Country	Young (%)	Country	Mid (%)	Country	Old (%)
Argentina	1.8	Argentina	0.5	Argentina	0.6
Australia	3.1	Australia	3.2	Australia	3.7
Belgium	0.5	Bulgaria	0.8	Bulgaria	1.2
Bulgaria	2.9	Canada	1.9	Canada	1.9
Canada	1.4	China	54.4	Switzerland	3.1
Switzerland	0.3	Colombia	0.5	China	40.1
China	59.5	Germany	0.5	Colombia	1.9
Colombia	2	Spain	0.3	Finland	0.6
Czech Republic	0.3	Finland	0.5	France	6.8
Germany	1.2	France	5.9	United Kingdom	3.7
Algeria	0.1	United Kingdom	4.6	Hungary	0.6
Egypt	0.1	Croatia	0.3	Italy	0.6
Spain	0.1	Israel	0.3	Japan	1.9
Finland	0.4	India	0.3	Korea	1.2
France	3.7	Italy	0.5	Lithuania	1.2
United Kingdom	2.6	Japan	0.8	Netherlands	1.2
Greece	0.1	Korea	0.8	Norway	0.6
Hong Kong	0.2	Lithuania	0.5	New Zealand	3.7
Croatia	0.5	Netherlands	2.4	Sweden	0.6
Indonesia	0.1	New Zealand	1.9	Slovakia	2.5
India	0.8	Serbia	0.5	United States	21.6
Italy	2	Sweden	0.3	South Africa	0.6
Japan	1.4	Singapore	0.3	**Total**	**100**
Korea	1.5	Slovenia	0.3		
Kuwait	0.1	Slovakia	3.8		
Lithuania	0.5	Thailand	0.8		
Morocco	0.1	United States	12.4		
Macedonia	0.1	South Africa	0.5		
Mongolia	0.1	**Total**	**100**		
Martinique	0.1				
Mexico	0.5				
Netherlands	1.1				
Norway	0.1				
New Zealand	1.4				
Peru	0.1				
Philippines	0.2				
Portugal	0.1				
Romania	0.1				
Serbia	0.5				
Saudi Arabia	0.1				
Sweden	0.1				
Slovenia	0.1				
Slovakia	3.1				
Turkey	0.3				
United States	4.9				
Mayotte	0.1				
South Africa	0.3				
Total	**100**				

Appendix B: European Medicines Agency (EMA) Approval Information

Therapy	Subtype	Reference Clinical Trial(s)	# of Participants (Interventional Arm)	Age Information	Response and Adverse Events Stratified by Age
Ibrutinib	CLL	Phase III PCYC-1115-CA trial for first line treatment.	269	Trial eligible to age 65 or older Median age 73 (65-90)	No
		Phase III PCYC-1102-CA trial for relapsed treatment.	51	Median age 68 (37-82) 64% age 65 or older	No
		Phase III PCYC-1112-CA study compared ibrutinib to ofatumumab monotherapy for relapsed treatment.	196	Median age 67 (30-88) 61% over age 65	No
		Phase III CLL3001 study investigated ibrutinib-rituximab-bendamustine (IBR) combination for relapsed treatment.	289	Median age 64 (31-86)	No
	MCL	Phase II PCYC-1104-CA trial for relapsed treatment.	111	Median age 68 (40-84) 63% age 65 or older	No
		Phase III PCI-32765MCL3001 study compared Ibrutinib monotherapy to Temsirolimus.	139	Median age 68 (34-88) 62% over age 65	No
	WM	Phase II trial name not given.	63	Median age 63 (44-86)	No
Obinutuzumab	CLL	Phase III BO21004/CLL11 study of obinutuzumab + chlorambucil for first line treatment.	333	Median age 73 44% over age 75	No
	FL	Phase III GALLIUM study of obinutuzumab in combination with chemotherapy for first line treatment.	699	Median age 57, age range not given	No
		Phase III GADOLIN study of obinutuzumab in combination with bendamustine for relapsed treatment.	194	Median age 63, age range not given	No
Venetoclax	CLL	Phase II M13-982 study of venetoclax monotherapy for relapsed treatment.	106	Median age 67 (37-83)	No
		Phase III MURANO study of venetoclax + rituximab for relapsed treatment.	194	Median age 65 (22-85)	No
CAR T Axicabtagene Ciloleucel	DLBCL	Phase I/II ZUMA-1 study in relapsed treatment.	101	Median age 58 (23-76) 24% over age 65	No
CAR T Tisagenlecleucel	DLBCL	Phase II CCTL019C2201 trial for relapsed treatment.	111	Median age 56 (22-76) Mean age 54 28% over age 65	No
Lenalidomide	MCL	Phase II MCL-002 trial for monotherapy relapsed treatment.	170	Mean age 68, age range not given	No

CLL = chronic lymphocytic leukaemia; DLBCL = diffuse large B-cell; FL = follicular; MCL = mantle cell; WM = Waldenstrom's macroglobulinaemia

Appendix C: Clinical Trial Analysis

	CLL	FL	DLBCL	MCL	WM
Phase II	204	226	280	194	83
Phase III	29	36	31	16	9
Total	**233**	**262**	**311**	**210**	**92**
Subtype Specific Trials	130	51	116	55	8
Novel Therapy Trials	214	223	256	181	77
Subtype Specific Novel Therapy Trials	124	43	97	51	7
First Line Novel Trials	51	34	40	31	8
Relapse Novel Trials	140	176	202	141	61
Novel CT Age Eligibility "Young"	208	221	249	176	77
"Young" % of all Novel Trials	**97%**	**99%**	**97%**	**97%**	**100%**
Novel CT Age Eligibility "Mid"	196	202	228	160	63
"Mid" % of all Novel Trials	**92%**	**91%**	**89%**	**88%**	**82%**
Novel CT Age Eligibility "Old"	177	183	208	135	60
"Old" % of all Novel Trials	**83%**	**82%**	**81%**	**75%**	**78%**
Novel CT "Old" Only	2	0	4	0	0
Novel CT "Mid" or "Old" Only	4	2	4	5	0

Copyright © 2018 Lymphoma Coalition. All rights reserved.

CLL = chronic lymphocytic leukaemia; DLBCL = diffuse large B-cell; FL = follicular; MCL = mantle cell; WM = Waldenstrom's macroglobulinaemia

Data as of October 2019

"Young" 18-59 years, "Mid" 60-69 years, "Old" 70+ years

Note: Not all clinical trial age requirement parameters fit perfectly into the age categories above. For example, trials with age eligibility 18-60 were coded as "young" only.

References

1. United Nations; DESA/Population Division. 2019 Revision of world population prospects. United Nations website **https://population.un.org/wpp**. Updated June 17, 2019. Accessed October 29, 2019.

2. Cleary M; ISPOR. Anticipating the impact of an aging world. *Value and Outcomes Spotlight*. 2019;5(5). ISPOR publication ISSN 2375-8678.

3. National Cancer Institute. Cancer stat facts: Non-Hodgkin lymphoma. Surveillance, Epidemiology, and End Results Program (SEER) website **https://seer.cancer.gov/statfacts/html/nhl.html**. Updated 2017. Accessed October 29, 2019.

4. Deckx L, van Abbema DL, van den Akker M, et al. A cohort study on the evolution of psychosocial problems in older patients with breast or colorectal cancer: Comparison with younger cancer patients and older primary care patients without cancer. *BMC Geriatrics*. 2015;15(79). doi:10.1186/s12877-015-0071-7.

5. Nguyen MH, Smets EMA, Bol N, et al. Tailored web-based information for younger and older patients with cancer: Randomized controlled trial of a preparatory educational intervention on patient outcomes. *Journal of Medical Internet Research*. 2019;21(10). doi:10.2196/14407.

6. Cordoba R. Care for geriatric patients with lymphoma. Lecture presented at: Lymphoma Coalition Global Summit; October 2, 2019; Barcelona, Spain.

7. Minerd, J. Clinical challenges: Aggressive lymphomas in elderly patients. Med Page Today website. **https://www.medpagetoday.com/clinical-challenges/asco-lymphoma/73414**. June 11, 2018. Accessed November 1, 2019.

8. Boekel LCV, Peek ST, Luijkx KG. Diversity in older adults' use of the internet: Identifying subgroups through latent class analysis. *Journal of Medical Internet Research*. 2017;19(5). doi:10.2196/jmir.6853.

9. Eurostat. Internet activities in the past three months by age group EU-28, 2016. Eurostat website **https://ec.europa.eu/eurostat/statistics-explained/index.php?title=File:Internet_activities_in_the_past_three_months_by_age_group_EU-28,_2016_(%25_of_internet_users)4.png.** Updated December 19, 2016. Accessed October 29, 2019.

10. Turner AM, Osterhage KP, Hartzler AL, et al. A closer look at health information seeking by older adults and involved family and friends: Design considerations for health information technologies. *In AMIA Annual Symposium Proceedings.* 2018; 2018 (1036).

11. Krok JL, Baker TA, Mcmillan SC. Age differences in the presence of pain and psychological distress in younger and older cancer patients. *Journal of Hospice & Palliative Nursing*. 2013;15(2):107-113. doi:10.1097/njh.0b013e31826bfb63.

12. Patterson P, Mcdonald FE, Zebrack B, Medlow S. Emerging issues among adolescent and young adult cancer survivors. *Seminars in Oncology Nursing*. 2015;31(1):53-59. doi:10.1016/j.soncn.2014.11.006.

13. Whelehan S, Lynch O, Treacy N, et al. Optimising clinical trial design in older cancer patients. *Geriatrics (Basel)*. 2018;3(3):34. doi:10.3390/geriatrics3030034

14. Morrison, V et al. Treatment approaches for older and oldest patients with diffuse large B-cell lymphoma – Use of non-R-CHOP alternative therapies and impact of comorbidities on treatment choices and outcome: A Humedica database retrospective cohort analysis, 2007–2015. *Journal of Geriatric Oncology*. 2019; 0(0). doi: **https://doi.org/10.1016/j.jgo.2019.07.025**.

15. Sano D et al. Safety of axicabtagene ciloleucel CD19 CAR T-cell therapy in elderly patients with relapsed or refractory large B-cell lymphoma. *Blood*. 2018; 132(96). doi: **https://doi.org/10.1182/blood-2018-99-120013**

16. Ratnasingam S, Casan J, Shortt J, et al. Cytarabine-based induction immunochemotherapy in the front-line treatment of older patients with mantle cell lymphoma. *Sci Rep*. 2019; 9(13544). doi: 10.1038/s41598-019-49776-9.

LYMPHOMA COALITION
Worldwide Network of
Lymphoma Patient Groups
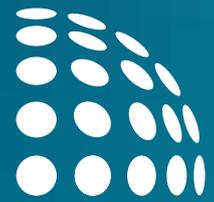
WWW.**LYMPHOMACOALITION**.ORG

know your subtype

To transform the lymphoma landscape ensuring patient centricity is defined by people affected by lymphoma in order to improve patient outcomes across all health system decisions.

This report is a valued product of the Lymphoma eInformation Project (LeIP)

Contact us if you are a patient organisation that focuses on lymphomas, including CLL, or if you are interested in starting a patient organisation.

E info@lymphomacoalition.org | T +1-905-990-0609

WORLD LYMPHOMA AWARENESS DAY – 15 SEPTEMBER.