PSY136

TOO OLD FOR TREATMENT: AGEISM IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL). A NARRATIVE REVIEW OF THE LITERATURE

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INTRODUCTION

- Chronic lymphocytic leukemia (CLL) is the most common leukemic disease in the Western World[1], with an incidence of 4.2/100,000 cases per year[2]. However, CLL is primarily a disease of the elderly, with a median age at diagnosis of 72 years[2]. Over the age of 65, the number of new diagnoses increases to 22-30/100,000[3], and to more than 30/100,000 cases beyond 80 years[2].
- Survival in CLL has significantly improved in recent years. Nevertheless, age-related disparities persist and many elderly patients currently receive suboptimal treatment[4], showing lower survival rates[5]. Greater awareness of this problem may improve survival for older patients with CLL.

OBJECTIVE

To review the literature relating age as a determinant of therapeutic decisions in CLL and search for evidence of ageism in the access to treatment of elderly patients.

METHODS

- Electronic databases [MedLine/PubMed] and grey literature [Google Scholar, congress proceedings, technical reports] were searched to identify publications investigating ageism in oncology to comprehensively address the complex problematic of age discrimination with a particular focus on 1) CLL treatment, 2) economic and social costs and 3) social value of the elderly. Studies in English or Spanish published until December 2015 were considered.

RESULTS

- A total of 31 publications were considered relevant to review (Figure 1).

Figure 1. Summary of literature search

Theme	Publications
Influence of age in decision making regarding CLL treatment[6-13]	8
Cost-of-illness on elderly[14-26]	13
The value of the contribution of older persons to society[27-36]	10

"Are older CLL patients getting the treatments they deserve?"

Influence of age in decision making regarding CLL treatment (Figure 2)

Figure 2. Age in CLL decision making

Currently	Goal
Lack of clinical evidence[7,35] •Clinical trials performed in individuals 10 to 15 years younger than median age at diagnosis of CLL (72 years)[7]. Therefore, there is no consensus on how to manage aged patients	**Inclusion** of older people with no age restriction **in clinical trials**
Age discrimination[35] •Elderly CLL patients (>70 years) are treated less effectively and frequently (p<0.001), and therefore have lower response rates (p<0.001), than younger ones[10] •Older patients with CLL do better emotionally than younger ones[6], being less depressed (p= 0.014) and with an increased emotional (p= 0.0001) and social (p= 0.002) quality of life. Moreover, they want to retain choice and control of decision making[28]	Treatment decision based on **performance status**, comorbidities or quality of life[27]
• Decision-making on the care and treatments mostly based on **chronological age**[8,27]	**Biological age** (health and functional status, comorbidities)[35]
Special health needs of elderly • Older age and/or high comorbidity burden are negative predictive factors to receive active therapy[9] • Survival for patients with chronic leukemias decreases with age. This decrease is relatively small until age 75 and is especially marked for patients age 85 and older[12]	Chemo-immunotherapy is more effective than chemotherapy in elderly population with high prevalence of comorbidity[11,21] **New targeted therapies**, based on small molecule inhibitors, are expected to be particularly useful in elderly patients with CLL, due to their efficacy[17] and non chemo-related toxicity[13]
• **Subjective Frailty Status**[8,29] / Too frail for treatment: low intensity treatment or palliative care[27]	**Frailty assessment**: Clinical condition, Short questionnaires (PRISMA), Functional tests (Timed up and go, slow gait speed)[29] Frailty management: Standardized patient evaluation (Comprehensive Geriatric Assessment, **CGA**[8,27,29])

Cost-of-illness on elderly

- CLL imposes a high economic burden, primarily driven by pharmaceutical[24] and inpatient costs[16-18] (Table 1).

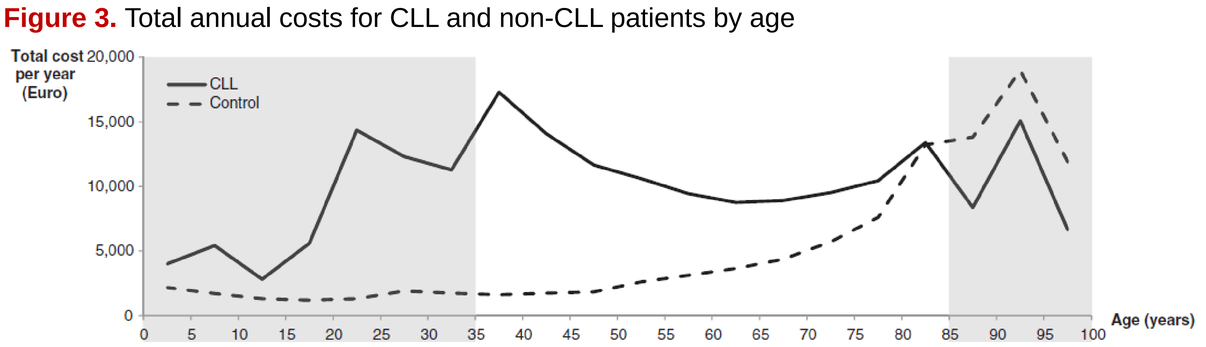
Table 1. CLL costs

Economic burden	Average lifetime costs/patient (compared to controls)	Annual cost/ patient[16-18,23]	Hospital aggregated charges/ year	Average length of hospital stay/ patient	Informal care (Non-Hodgkin Lymphoma)	Non-medical costs (Outpatient Chemotherapy)
€366-€425 million/ year[17,23]	€30,056[20]	From €2,632 in Ukraine[18] to €7,636 in Germany[17]	€209 million[24]	7.8 days/year[25]	>10 hours/day[19]	45% Out-of-pocket, 55% wages lost[26]

All costs were updated to 2016 Spanish Euro using the 'CCEMG – EPPI-Centre Cost Converter' (v.1.5 last update: 29 April 2016).

- High pharmaceutical costs attributable to the rapid emergence of new healthcare technologies[14]. Cost-effectiveness ratio of innovative treatments for hematologic malignancies has been stablished in $50,000 – 100,000/QALY[15]. In this sense, health care policymakers should ensure affordable treatment and make certain cost considerations to not deprive patients from life-prolonging therapy[14,22].
- The costs of the disease differ by age group[17]. The average yearly cost for each CLL patient increases with advancing age (>65), while for non-CLL patients they increase steadily until the age of 85, with the cost difference decreasing to zero at 85[17] (Figure 3). Younger patients are more extensively treated for CLL to increase their chances of survival. Costly procedures might be used only for patients under the age of 66[17].

Figure 3. Total annual costs for CLL and non-CLL patients by age

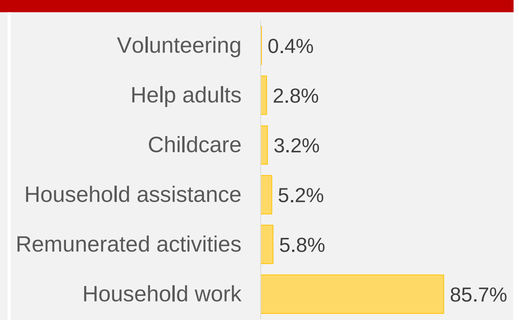
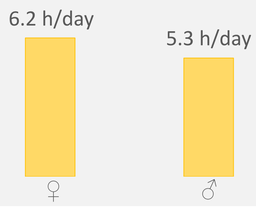


Adapted from Blankart et al.[17]

The value of the contribution of older persons to society

- While ageing presents challenges to society, it also creates many opportunities[34]. The social contribution of older people mainly occurs in terms of unpaid support (informal work, volunteering or within the family), representing 8.5%[32]-10.4%[30] of the gross domestic product (GDP) in Spain (Table 2). This contribution can be fostered by helping them to maintain good health[34].

Table 2. Contribution of older people

Activity	Value	Distribution/contribution
Domestic sphere and volunteering[30,31]	Additional services for the economy and society, generating more **welfare**[31]	
	Family support • 50% of Grandparents care for grandchildren everyday[31] • 24.9% of Grandparents care for grandchildren when parents are at work[33]	
	Volunteering[36]	• £10 billion per annum (UK) • Annual average 104.6 and 54.5 h of informal and formal volunteering, respectively, per person over 65 (UK)
Spending power[32,36]	**Economic contribution**, job creation	• Leisure consumption[32]: €8,000 million or 0.9% of GDP (Spain) • Spending power of £76 billion in 2010 and predicted in £127 billion in 2030 (UK)[36]
Provision of social care[33,36]	**Informal care**[33] **Social care**[36]	• 30.7% of elderly • Delivered benefits of £34 billion in 2010 and predicted in £52 billion in 2030 (UK)

CONCLUSIONS

- Older CLL patients are undertreated when compared to younger ones, while costly procedures are mainly offered to patients under the age of 66. Although it is irrefutable that some health changes appear with age, "advanced" age alone should not be a contraindication for treatments that can improve patient's survival or quality of life. On the other hand, older people make a significant contribution to society, which can be fostered by helping them maintain good health.

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