**Costs related to frontotemporal dementia in Latin America: a scoping review of economic health studies**

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**Abstract**

**Objective**: Describe the costs related to Fronto-Temporal Dementia (FTD) in Latin-American (LA) countries.

**Introduction**: FTD is a complex syndrome characterized by changes in behavior, language, executive control, and motor symptoms. Its annual economic burden per patient in developed countries has been classified as considerable, amounting to US$119,654 per patient, almost double the patient's costs reported for AD. However, there is little information regarding Cost-of-illness (COI) for FTD in LA. We expect this to be higher as its budget represents only 0.001% of the total budget of the health sector in most LA. Therefore, our objective in this systematic review was to describe the costs related to FTD in LA countries.

**Inclusion criteria**: We will include COI observational studies on FTD conducted in Latin American countries and published in English, Spanish, or Portuguese from inception to September 2020.

**Methods**: We will perform a systematic search in Pubmed / Medline, Scopus, Web of Science, Scielo, Cochrane and gray literature. Studies will be selected by two independent authors, with a third author participating in discrepancies. Data will be then extracted. For quality assessment, we will use a COI assessment tool available in the literature. All costs will be reported in USD for one month and adjusted for inflation.

**Keywords**: Dementia, Frontotemporal Dementia, Costs, and Cost Analysis, Systematic review, Latin America

**Introduction**

Fronto-Temporal Dementia (FTD) is a complex syndrome characterized by clinical disorders that include progressive changes in the functions of behavior, language, executive control, and motor symptoms; associated with anterior and frontal temporal lobe degeneration (1,2). This dementia includes three different clinical phenotypes: behavioral variant of a primary progressive aphasia (bvPPA), semantic variant (svPPA), and non-fluent / agrammatic variant of PPA; the most common being the behavioral variant of FTD (bvFTD)(3).

Worldwide, FTD represents up to 5-6% of all dementias. Although less frequent than Alzheimer's disease (AD) (2,4,5), it is the second most common dementia in people under 65. FTD has an incidence of 1.61/100,000 and mortality of 1.56/100,000 person-years (6). It is considered early-onset dementia since it can present with an incidence of up to 10.8/100,000 people with a peak between 65 and 69 years of age (2,7). In Latin American (LA) communities, FTD prevalence rates of 1.2-1.8 / 1000 people have been described in populations over 60 years of age in Venezuela, Peru, and Brazil (8).

According to the WHO, the societal cost of dementia worldwide was US$818 billion in 2015, equivalent to 1.1% of global gross domestic product (GDP). Consequently, some reports classify the annual economic burden per patient of DFT as considerable, amounting to US$119,654 per patient, which could almost double the patient's costs reported for AD (9). In developed countries, where the annual income is high, this cost is mainly justified by expenses related to productivity since a patient can reduce their annual income by up to US$ 50,000 after twelve months of diagnosis due to lost workdays and early layoffs (9). In LA, the expected socioeconomic impact of the FTD will be much more significant since the health budget allocated to this type of disease is small and may represent only 0.001% of the total budget and 0.02% of the budget allocated to the health sector. Additionally, precarious labor systems assign low wages compared to those in developed countries, which generates more significant uncertainty regarding the costs associated with FTD in the region.

The cost of illness (COI) is defined as the value of resources spent or abandoned because of a health problem. It includes the costs of the health sector (direct costs), the value of productivity diminished or lost by the patient (indirect costs), and the cost of pain and suffering (intangible costs) (10,11). Direct costs for the health sector include hospital expenses (hospitalization, treatment, and medical care) and, also, non-reimbursable expenses incurred by patients and family members concerning health care (medications, transportation for hospital visits, home modifications because of illness, and costs of caring for the patient at home). On the other hand, indirect costs can result from lost wages or benefits due to illness, premature death, side effects of illness or treatment, or time spent receiving treatment. Indirect costs also affect family members who reduce or cease employment to care for the patient (10).

Although its calculation is complicated, COI analysis provides essential information on the disease's financial impact to make more efficient use of resources (for example, select a specific treatment strategy) by health managers, researchers, and medical specialists. However, most studies on the economic burden of disease focus only on direct medical costs, as they are the easiest to identify for the health sector, which underestimates the total cost of the disease.

**Review Question**

What are the disease costs associated with frontotemporal dementia in Latin America?

**Inclusion Criteria**

**Population**

Patients with fronto-temporal dementia in Latin-America.

**Concept**

Financial burden

**Context**

As new research highlights the enormous cost of dementia and its distribution worldwide, evidence-synthesis becomes necessary to inform the decision of policy makers. Ideas like publicly funded long-term care services or long-lasting effective interventions to support families and reduce dependence must be informed by the cost of the disease. However, currently there are no systematic reviews assessing the cost of dementia, specifically fronto-temporal dementia, in Latin-American countries.

**Types of studies**

**Inclusion**

Studies that assess costs of disease, such as cross-sectional or cohort studies will be screened.

We will include studies that fulfill the following criteria:

- Studies that evaluated the cost-of-illness of fronto-temporal dementia in Latin-American population

- Studies that evaluated other type of economic studies of the cost-of-illness of fronto-temporal dementia in Latin-American population

**Exclusion**

We will exclude the next type of studies:

-Review articles, Abstracts, Letters, Editorials

-We will exclude studies written in languages other than English, Spanish or Portuguese

**Methods**

**Search strategy**

We developed the search strategy from Medical Subject Headings - MeSH (Pubmed) for "Frontotemporal dementia" and related words for "Cost of the illness," "Cost-Benefit Analysis," and "Economics," employing a PICO structure approach. We will include studies conducted in Latin American countries and published in English, Spanish, or Portuguese. We will limit the search date from inception to 2020.

**Information sources**

We will search the following databases: MEDLINE (accessed through Pubmed), Scopus, Web of Science and Embase with a supplementary search in the Health Economic Evaluations Database (HEED) for additional studies. We will adapt the search strategy for each of the databases.

Additionally, we will carry out a manual search in the repositories of the WHO and the world bank. We will also review the references of included studies in order to identify studies which might fulfill inclusion criteria.

**Study selection**

Before selecting studies, we will remove duplicate records and subsequently perform a manual review. We will select studies with Endnote x9 software by reviewing titles and abstracts to identify potentially relevant documents according to the inclusion criteria. Finally, these potential documents will be evaluated in full text to assess their eligibility. Two independent authors (MM & ARC) will make the selection, and a third author (CAD) will participate if there is any discrepancy through discussion and consensus.

We will include those studies of socioeconomic evaluations that provide data on the disease's costs by FTD. We will exclude publication types such as letters, notes, conference papers, short surveys, and clinical trials, as well as studies not available in full text.

Two authors (MM & ARC) will carry out data collection independently using a standardized form in Microsoft Excel. A third author (VVR) will verify the quality of the data before analysis. We will adjust the costs for inflation using the Consumer Price Index inflation calculator by the US Bureau of Labour Statistics for all costs reported in US Dollars.

**Assessment of methodological quality**

**Instrument**

The studies' quality will be critically assessed using a COI assessment tool developed by Afroz et al. (12). Two researchers (MM & ARC) independently will assess the risk of bias for each outcome.

**Calculation of domain scores**

This tool (12) has 15 indicators, which can be given no score, 0, a partial score of 0.5, or a total score of 1. Thus, it has a maximum obtainable score of 15. However, three items are specific to the disease used for its development and do not apply to our studies. Because of this, the maximum obtainable score will be 12.

**Data extraction**

The data extracted will include: Author, year of publication, Country, number of patients included in the study and the analysis, data collection method, calculation of costs, and quality of the articles. We will categorize the cost components into direct medical costs and indirect costs. The first one will be made up of medication costs, healthcare services, and additional direct costs, while indirect costs will include caregiver expenses, loss of productivity, and time loss due to patient care.

**Analysis of the evidence**

If possible, a meta-analysis will be performed. This will be done using a random effects model with DerSimonian and Laird weights. Heterogeneity will be tested with the Cochran Q statistic and quantified with the I2 statistic, which describes the variation in the effect size that would be attributed to the heterogeneity between studies, where an I2 value greater than 50% would indicate significant heterogeneity. Also, according to the number of included studies, publication bias will be evaluated and a p-value in two-tailed tests will be considered statistically significant.

**Data presentation**

Two tables will be developed summarizing both the characteristics of the included studied and the costs and its respective categories, respectively. If a meta-analysis is performed, this will be presented through a Forrest plot and publication bias will be graphed using a funnel plot.

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**Conflict of interest**

The authors declare no conflict of interest.

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