

# RETINOBLASTOMA IN LESS DEVELOPED COUNTRIES

## A SYSTEMATIC REVIEW

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# The problem:



- Little information about retinoblastoma in clinical findings and outcome at less developed countries (LDC) is published in the international peer-reviewed literature
- We speculated that patients present with advanced disease which may be associated to socioeconomical factors in LDC and there may be additional important data published at other sources in other languages than English

# Our approach



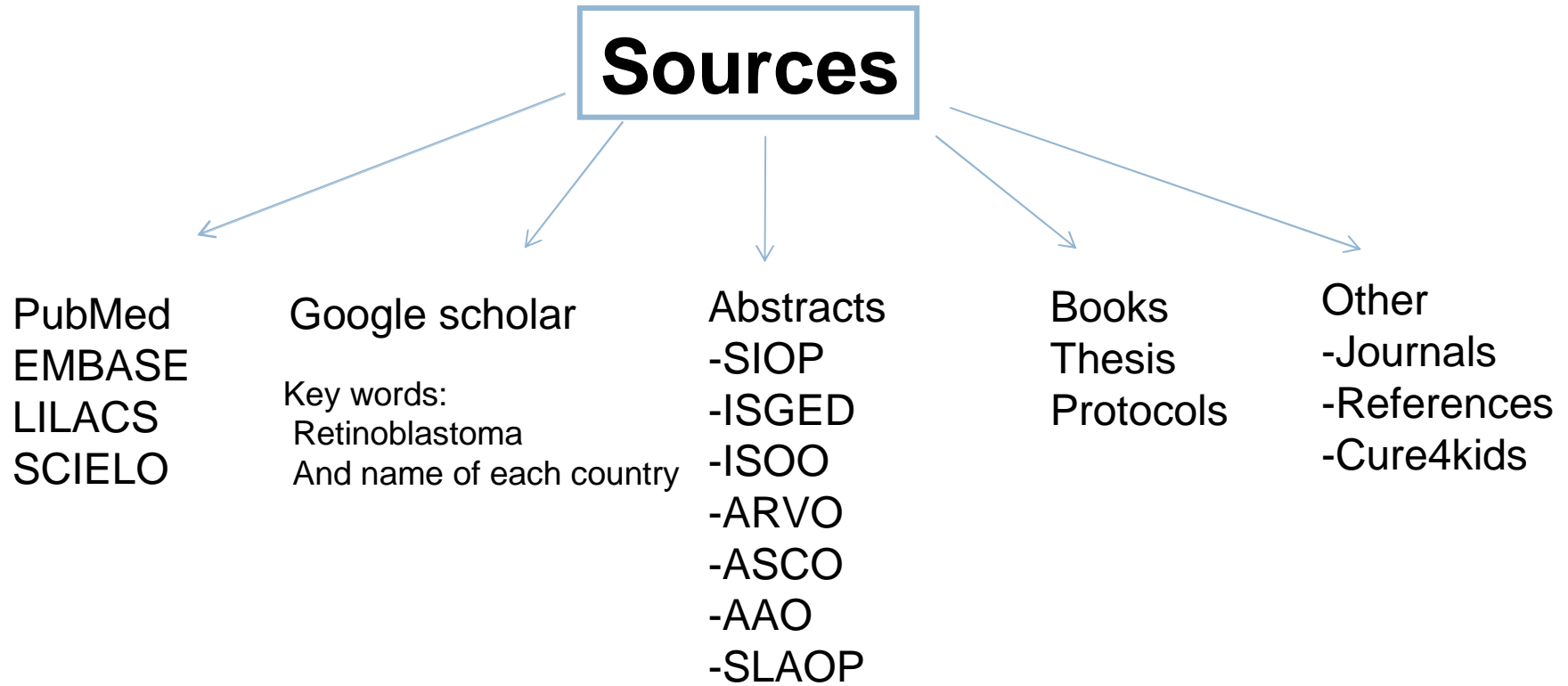
- ❑ Global systematic review
- ❑ Multinational, multilingual co-authors
- ❑ Data in Spanish, Arabic, Russian, Chinese, French, Turkish, Portuguese were analyzed
- ❑ Extensive literature search
- ❑ Local journals and abstracts
- ❑ Systematically collected data about demographics, clinical presentation, treatment and outcome from less developed countries
- ❑ Interval: January 1998-December 2007

# Methodology



- Discussion of study objectives
- Agreement of a data capture form in English
- Literature search (key word: Retinoblastoma, interval 1998-2007)
- Retrieved data was transferred to the data capture form in English
- A single database was created with eligible papers

# Methodology



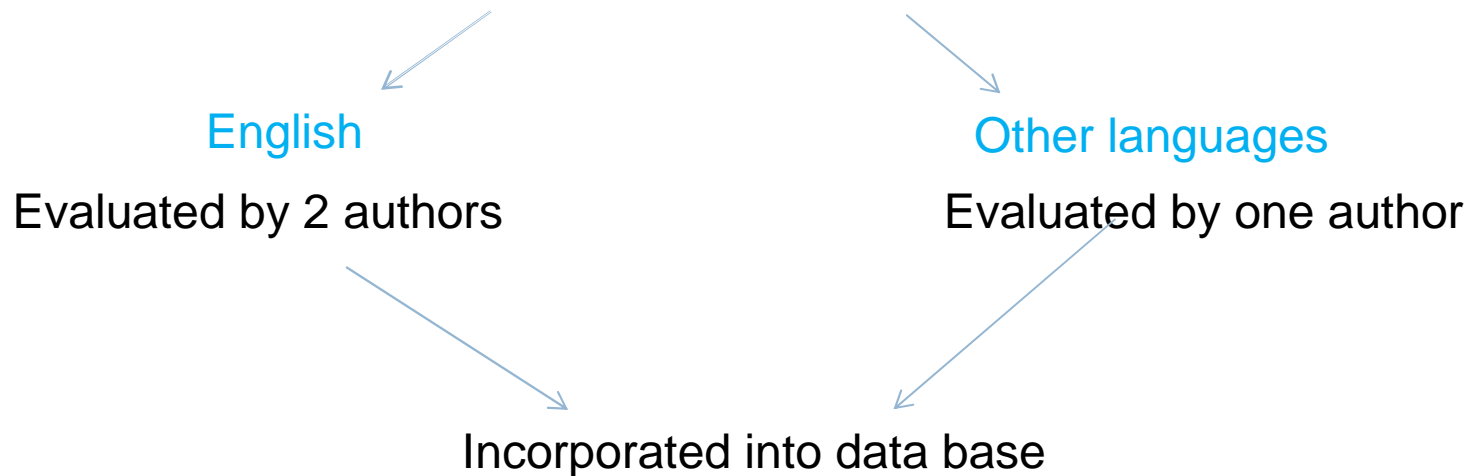
# Information retrieved

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- **Setting:** Country, city, center description
- **Design:** Retrospective/prospective, type of paper
- **Clinical:** Presentation, % extraocular, staging used
- **Treatment:** Chemotherapy, radiotherapy, etc
- **Outcome:** Survival
- **Social problems:** Abandonment, lost to follow up, treatment refusal
- **Special data:** Chemoreduction programs, public awareness campaigns

# Data extraction

## Identification of potential papers



- ✓ Data base analyzed by 2 authors
- ✓ Data evaluated to eliminate duplication
- ✓ Discussed with regional authors for consistency
- ✓ Statistical analysis
- ✓ The final database was constructed in a way that each country had a calculated single value for each parameter

# Definitions;



- Countries classified according to World Bank for the year 2000 as;
  - LIC (Low-income countries)
  - MIC (Middle-income countries, both upper and lower)
- \*\*Gross National Income per capita
- Socioeconomical and health-related indicators were obtained from World Health Organisation(WHO)
- Human Development Index(HDI) was obtained from UN Development programme

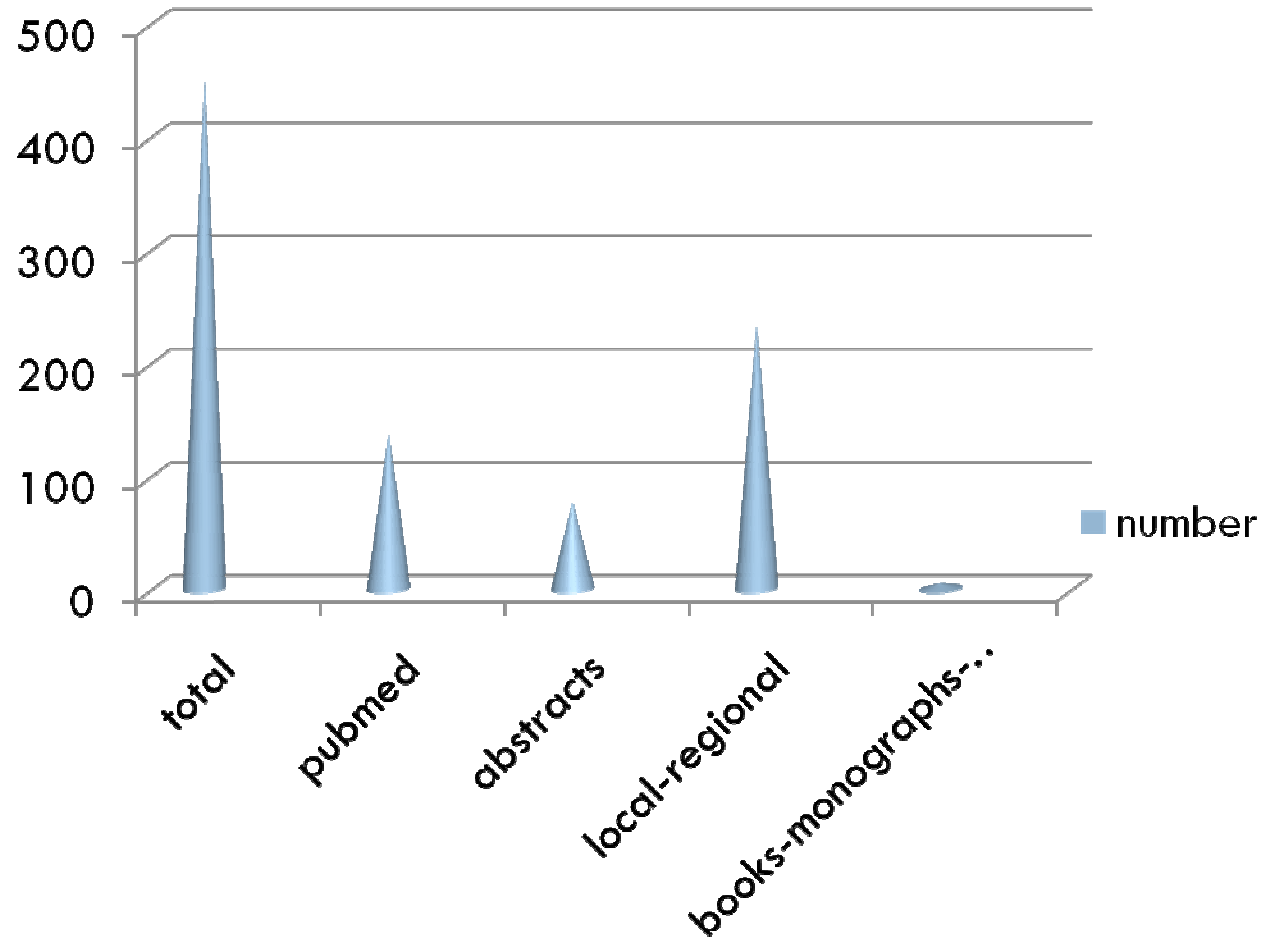
# Socioeconomical data



- Gross Domestic Product (GDP)
- Human Development Index (HDI)
- Per capita health expenditure
- Infant mortality rate
- Per capita health expenditure
- % per capita health expenditure as a % of total expenditure
- Maternal mortality rate
- Vaccinations (% DPT3 at 1 year)
- Fertility rate

# Results reference retrieval

- Total n= 456
- PubMed available literature n=138
- Abstracts to meetings=78
- Local-regional publications=235
- Books-monographs-protocols=5



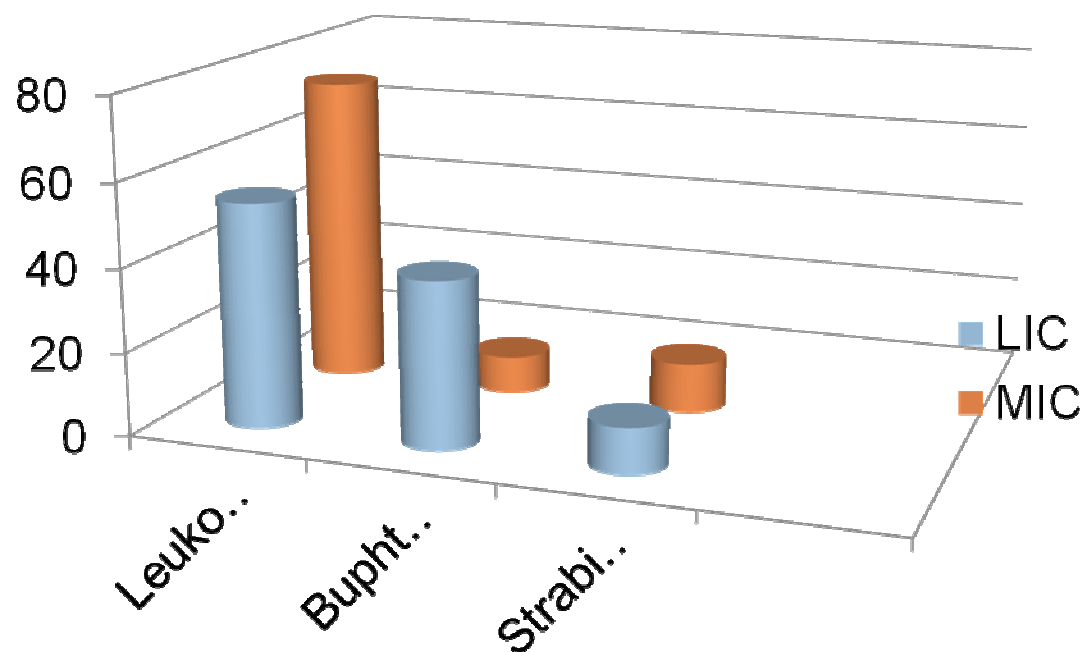
# General data

## After analysing the duplicated data;

- **References; 164**
  - 44(27.5%) Pubmed
  - 120(72.5%) Other sources
    - 59(49.1%) abstracts
    - 50(41.7%) local publications
    - 11(9.2%) books, thesis, web-only..
- **Patients: 14,733**
- **Language:**
  - ▣ English 73.5%
  - ▣ Other 26.5%
- **Countries :**
  - ▣ LIC 12
  - ▣ MIC 36

# Clinical presentation;

- 22 countries,
- 4671 patients
- Leukocoria: 70%  
(LIC : 54, MIC: 74)  
 $p=0.14$
- Buphthalmia/orbital  
mass: 18%  
(LIC: 40.5, MIC: 9)  
 $p=0.006$
- Strabismus: 11%  
(LIC: 11, MIC: 12)  
 $p=0.022$



# Results;

## Survival

- LIC → 40%(range 23-70)
  - Lower MIC → 77%(range 60-92)
  - Upper MIC → 79%(range 54-93)
- p=0.001

## Treatment refusal

- LIC → 35%(range 30-50)
  - Lower MIC → 11%(range 1-37)
  - Upper MIC → 5%(range 1-25)
- p=0.002

# Socioeconomical and health-related variables related to estimated survival

VARIABLE	N countries	R Pearson	R <sup>2</sup>	p
HDI	36	0.887	0.787	<0.0001
GDP	36	0.556	0.309	<0.001
HEALTH EXPENDITURE	35	0.554	0.307	0.01
DPT3	36	0.614	0.377	<0.0001
FERTILITY RATE	36	0.764	0.584	<0.0001
INFANT MORTALITY	36	-0.861	0.714	<0.0001
< 5 y. MORTALITY	36	-0.852	0.726	<0.0001
MATERNAL MORTALITY	35	-0.825	0.681	<0.0001
ADULT LITERACY	35	0.609	0.371	<0.0001

# Socioeconomical and health-related variables related to treatment refusal

VARIABLE	Countries	R Pearson	R <sup>2</sup>	p
HDI	22	-0.729	0.531	<0.0001
GDP	22	-0.440	0.194	0.04
HEALTH EXPENDITURE	21	-0.592	0.350	0.005
DPT3	22	-0.616	0.380	0.002
FERTILITY RATE	22	0.630	0.397	0.002
INFANT MORTALITY	22	0.696	0.484	<0.0001
<5y MORTALITY	22	0.704	0.496	<0.0001
MATERNAL MORTALITY	22	0.779	0.607	<0.0001
ADULT LITERACY	22	-0.629	0.396	0.002

## Socioeconomical and health-related variables related to the occurrence of metastatic disease

VARIABLE	Countries	R Pearson	R <sup>2</sup>	p
HDI	38	-0.780	0.608	<0.0001
GDP	38	-0.503	0.253	<0.001
HEALTH EXPENDITURE	35	-0.381	0.145	0.024
DPT3	38	-0.625	0.390	<0.0001
FERTILITY RATE	38	0.717	0.514	<0.0001
INFANT MORTALITY	38	0.721	0.520	<0.0001
< 5 Y. MORTALITY	38	0.754	0.569	<0.0001
MATERNAL MORTALITY	37	0.783	0.613	<0.0001
ADULT LITERACY	37	-0.409	0.167	0.012

# Multiple regression analysis



- For survival: Maternal mortality  $p < 0.0001$
- For metastatic disease: HDI  $p < 0.0001$
- For treatment refusal:
  - ▣ Maternal mortality  $p < 0.0001$ ,
  - ▣ Health expenditure  $p < 0,0001$ ,
  - ▣ Infant and  $< 5$  years mortality  $p = 0.002$ ,
  - ▣ GDP  $p = 0.02$

# Conclusions



- Grey literature provided substantial information
- Proptosis is the second presenting sign worldwide
- Treatment refusal and abandonment is a critical problem
- Socioeconomical indicators related to maternal and infant health are associated to poorer survival
- Our data may be used as baseline for future prospective studies