



# HOW TO WRITE A CLINICAL PROTOCOL

**Márcio Debiasi, MD, PhD**

Scientific Director

Curitiba, Junho/2016

---

# MÁRCIO DEBIASI - CV

- 2005: graduated Medical School → UFCSPA, Brazil
- 2009: Internal Medicine board certificate → HNSC, Brazil
- 2012: Medical Oncology board certificate → HSL, Brazil
- 2012: MSc - Epidemiology → UFRGS, Brazil
- 2013: Fellow at “The Breast Cancer Clinic” – U. of Chicago, EUA
- 2016: PhD - Epidemiology → UFRGS, Brazil
- Current Positions:
  - Medical Oncologist → HSL and HCMD, Brazil
  - Member of “Cochrane Collaboration”
  - Scientific Director of LACOG

# Structure and Facilities

## LACOG Coordinating Office

Study Design

Regulatory process



Statistics

Monitoring  
Audits

CRF and  
database

Communication

Porto Alegre, Brazil

# LACOG Membership Status

145 members



15 countries



---

# Clinical Protocol / Guideline

---

# Clinical Protocol / Guideline



---

# Clinical Protocol / Guideline

**WHY?**



---

# Clinical Protocol / Guideline

▣ **Cancer is a global Epidemic**

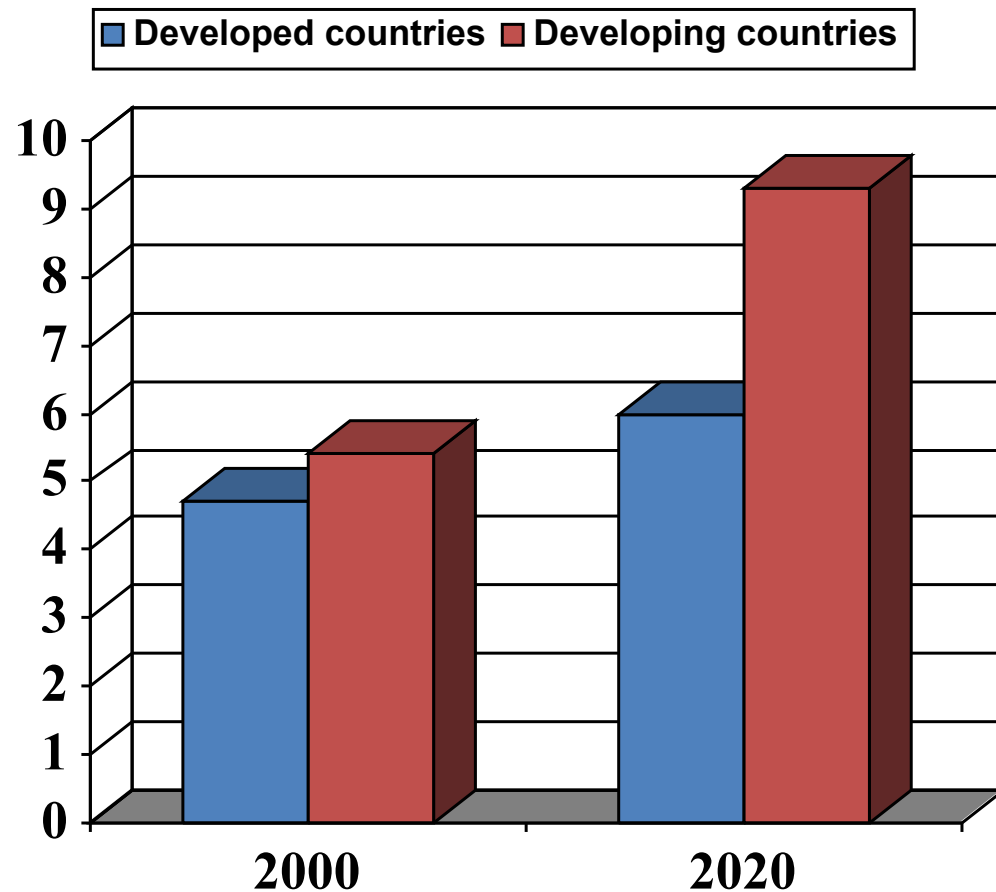


# Cancer: a Global Epidemic

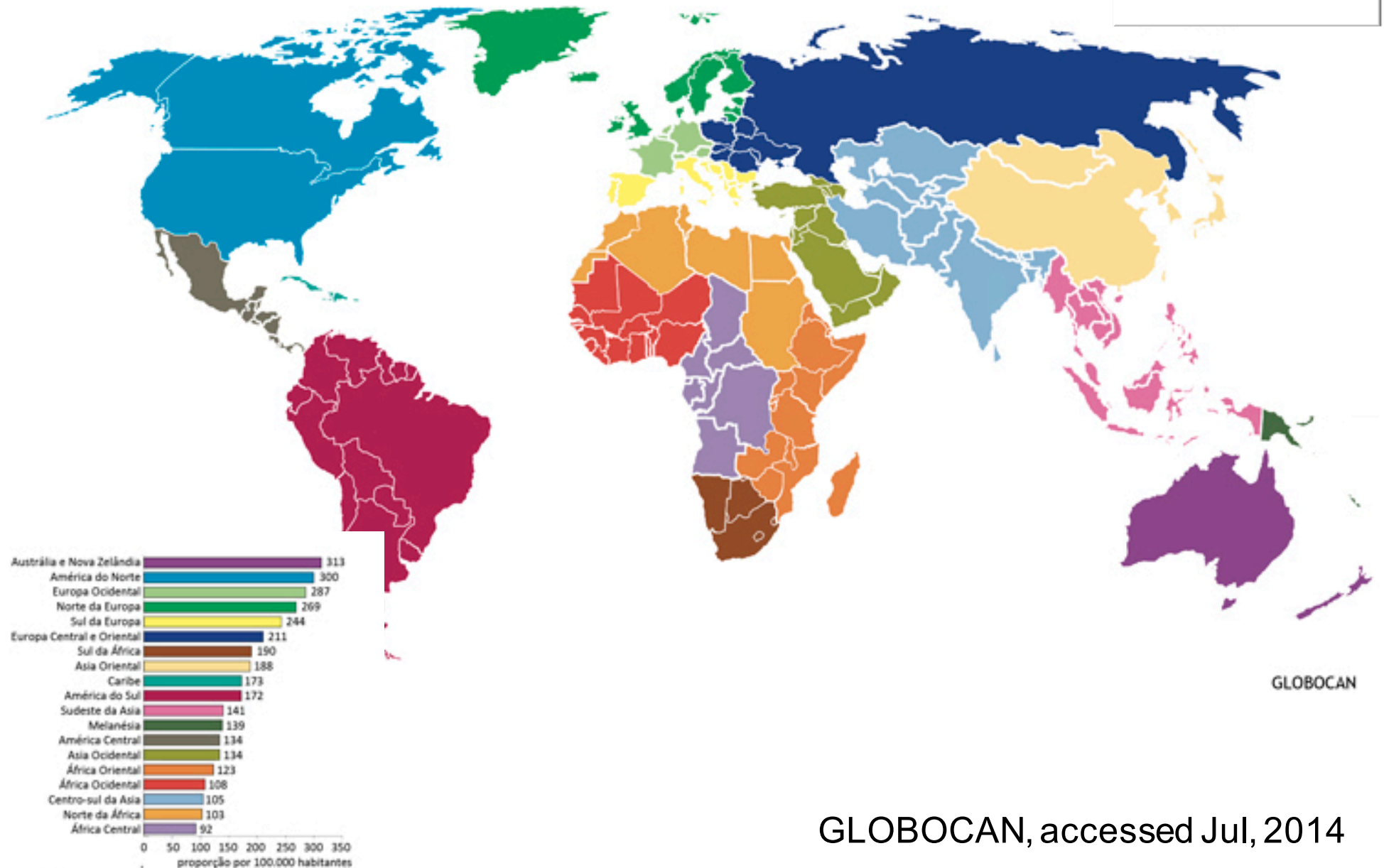
50% increase in new cancer cases up to 2020

Higher increase rates in low and middle income countries

## Cases (millions)



# Worldwide Cancer Incidence



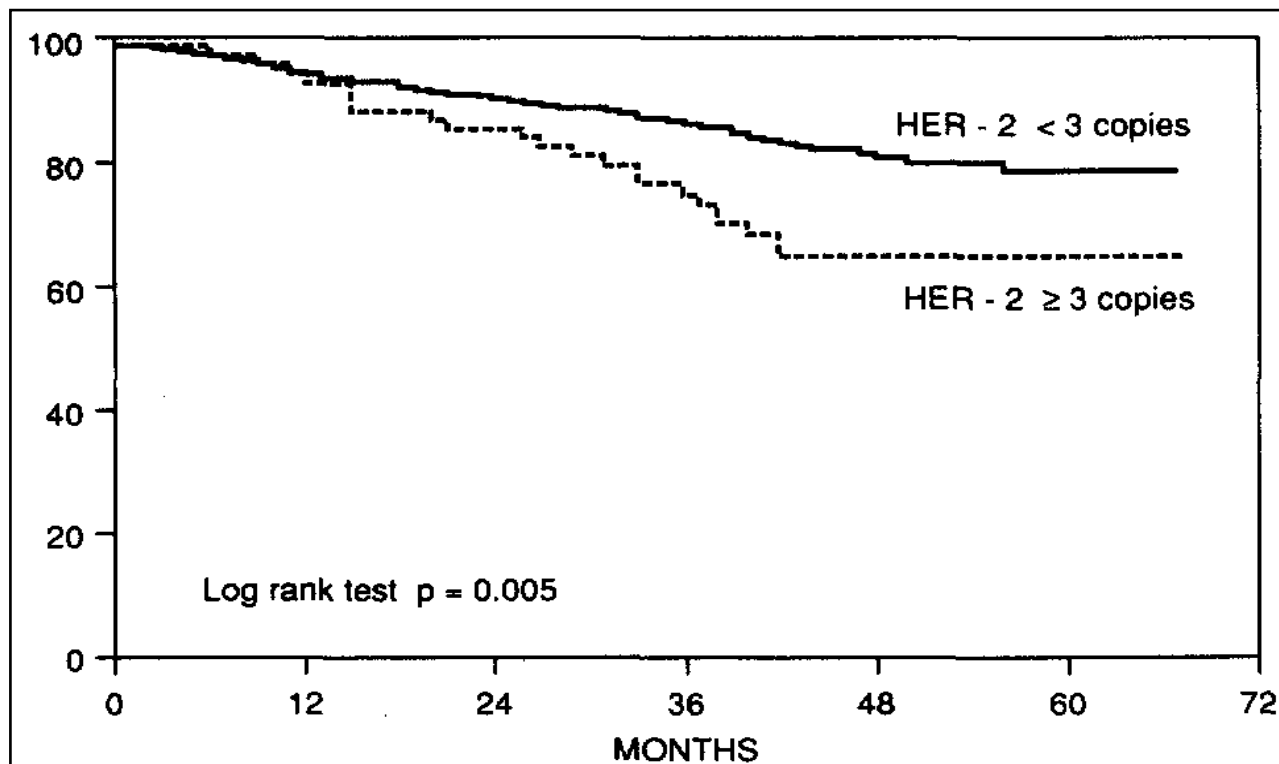
GLOBOCAN, accessed Jul, 2014

---

# Clinical Protocol / Guideline

- Cancer is a global Epidemic
- **Effective treatments, but complex and confuse evidence**

# HER2-positive Breast Cancer

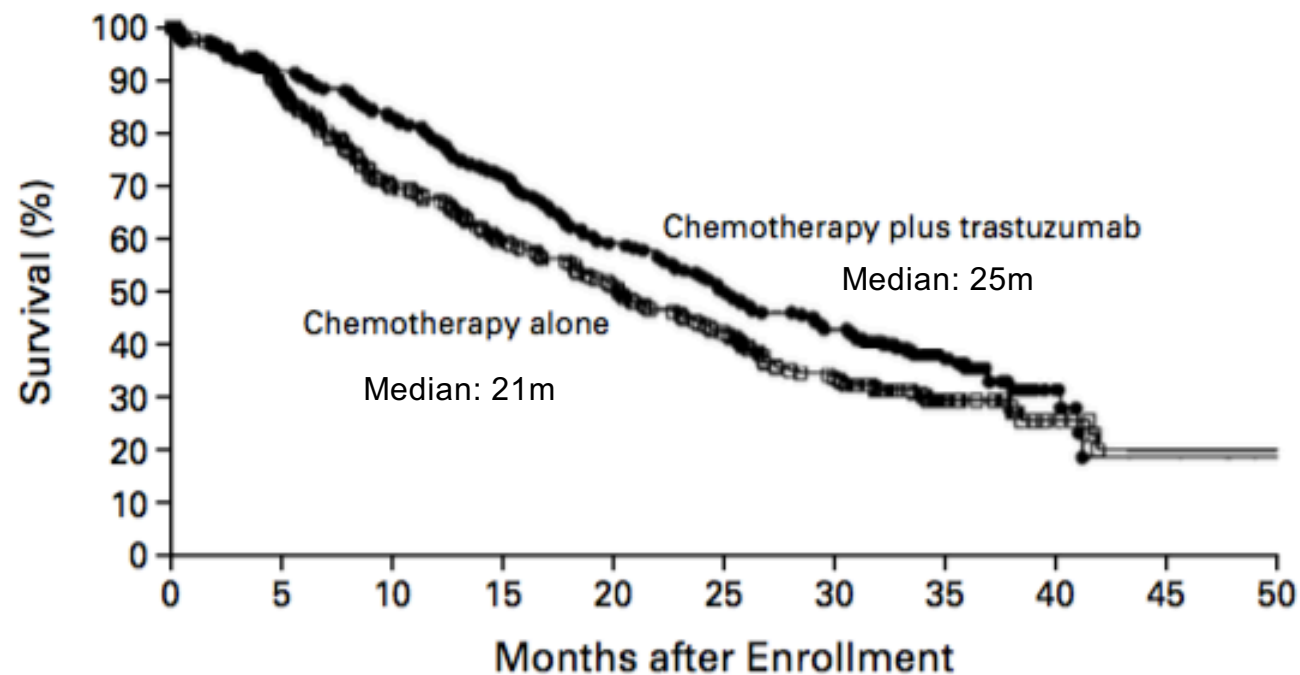


**Fig 4. Kaplan-Meier univariate analysis for OS in node-positive patients. (—) Patients with HER-2/neu copy number < 3; (· · · ·) patients with HER-2/neu copy number ≥ 3.**

Science 1987;235(4785):177-82.  
J Clin Oncol 1993;11(10):1936-42  
Clin Breast Cancer 2004;5(1):63-9.

# HER2-positive Breast Cancer

A



No. AT RISK

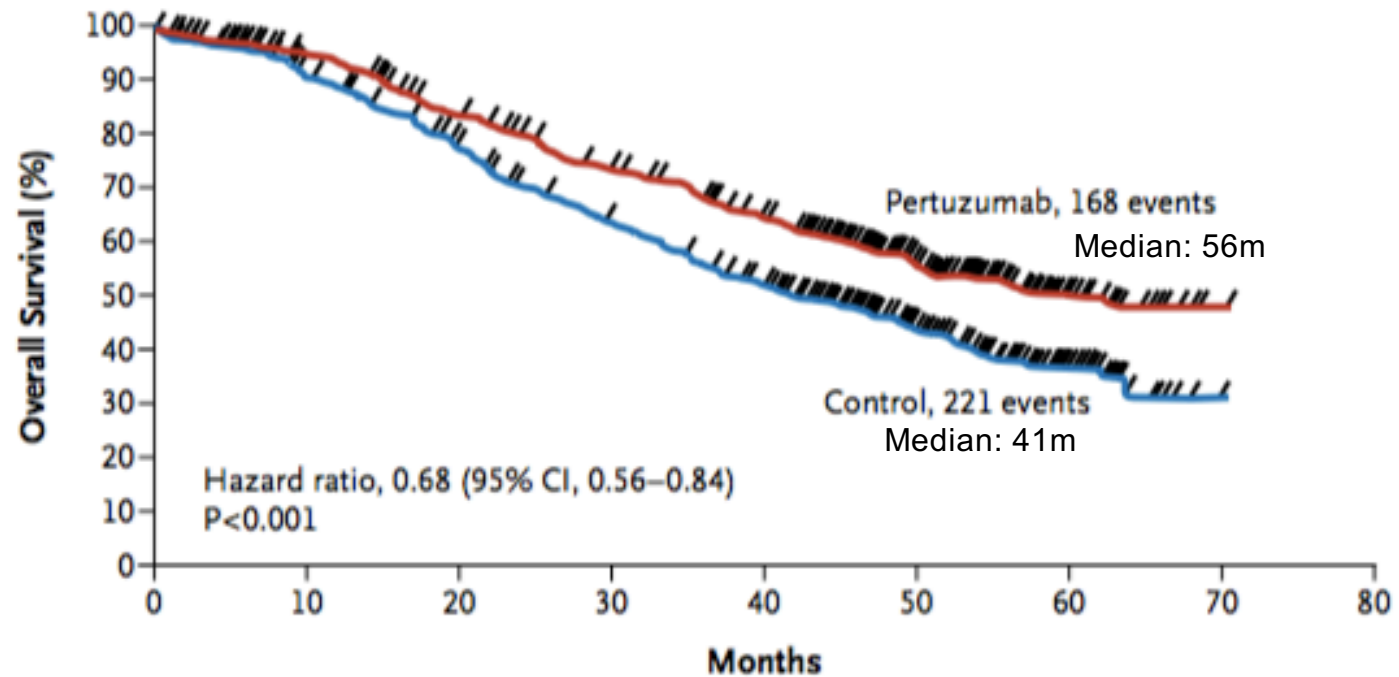
Chemotherapy  
plus trastuzumab  
Chemotherapy alone

235	214	192	165	134	114	96	47	11
234	205	160	136	116	97	76	37	13

NEJM 2015;372:724

# HER2-positive Breast Cancer

## A Overall Survival



### No. at Risk

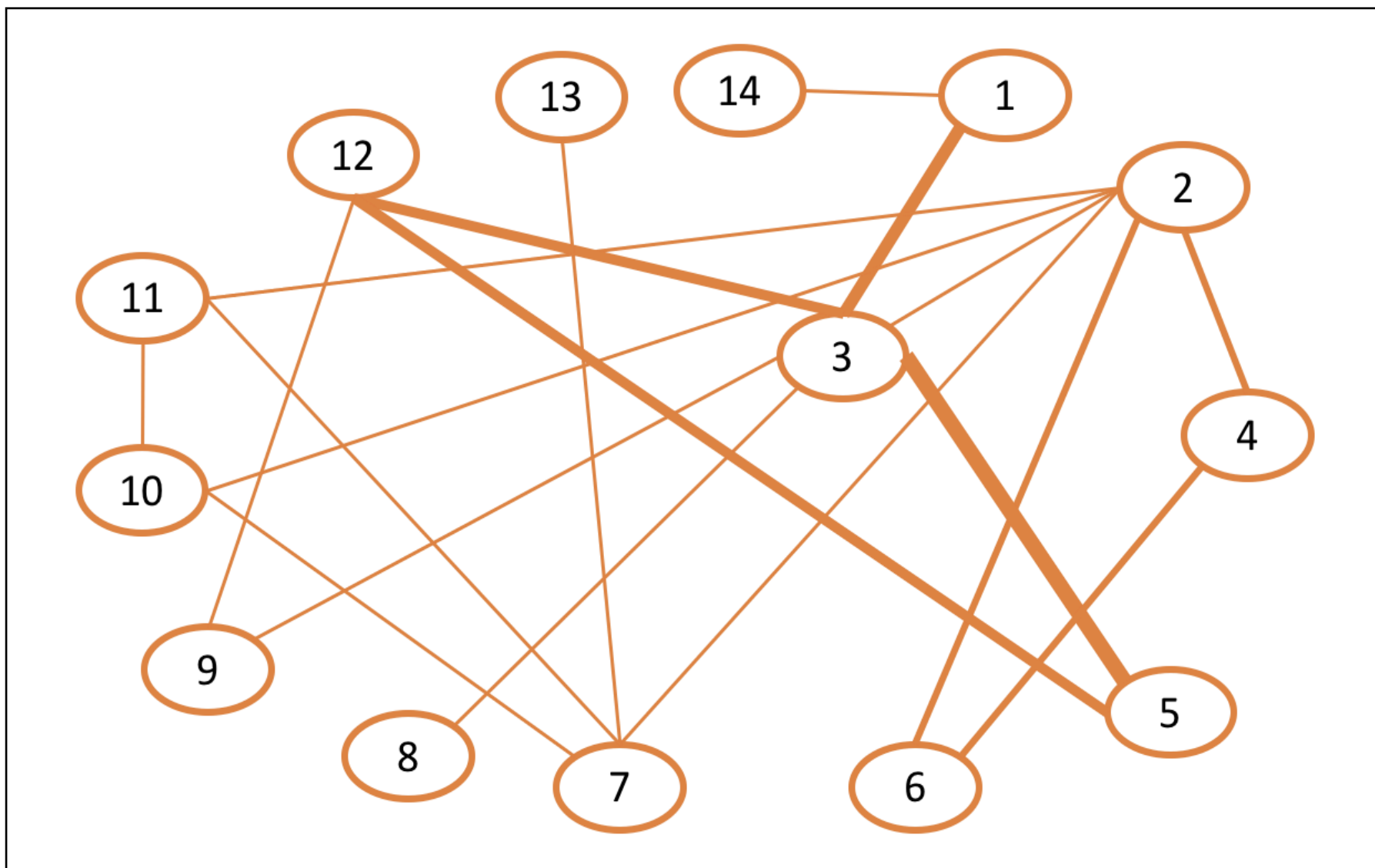
Pertuzumab	402	371	318	268	226	104	28	1	0
Control	406	350	289	230	179	91	23	0	0

NEJM 2001;344(11):783.  
NEJM 2015;372:724

## REDE RESPOSTA PATOLÓGICA COMPLETA:

- 17 ECRs – 4.383 pacientes
  
- Braços de tratamento
  - 1) QQUER QUIMIO SEM TERAPIA ANTI-HER2
  - 2) TAXANO + TRASTUZUMABE
  - 3) ANTRACÍCLICO + TAXANO + TRASTUZUMABE
  - 4) TAXANO + LAPATINIBE
  - 5) ANTRACÍCLICO + TAXANO + LAPATINIBE
  - 6) TAXANO + TRASTUZUMABE + LAPATINIBE
  - 7) TAXANO + TRASTUZUMABE + PERTUZUMABE
  - 8) ANTRACÍCLICO + TAXANO + TRASTUZUMABE sc
  - 9) ANTRACÍCLICO + TAXANO + CARBO + TRASTUZUMABE + LAPATINIBE
  - 10) TRASTUZUMABE + PERTUZUMABE
  - 11) TAXANO + PERTUZUMABE
  - 12) ANTRACÍCLICO + TAXANO + TRASTUZUMABE + LAPATINIBE
  - 13) ANTRACÍCLICO + TAXANO + TRASTUZUMABE + PERTUZUMABE
  - 14) TAXANO + CARBO + TRASTUZUMABE

## REDE RESPOSTA PATOLÓGICA COMPLETA: DESENHO





---

# Clinical Protocol / Guideline

- Cancer is a global Epidemic
- Effective treatments, but complex and confuse evidence
- **Judicialization**

---

# Judicialization

■ The case of England ...

# Judicialization

## ■ The case of England ...

- Ann Marie Rogers  
against NHS, England,  
2006



[http://news.bbc.co.uk/2/hi/uk\\_news/england/wiltshire/7926320.stm](http://news.bbc.co.uk/2/hi/uk_news/england/wiltshire/7926320.stm)

---

# Judicialization

- The case of England ...
- BRAZIL: increase in lawsuits

# Accepted for publication

JGO/2016/005678 - Manuscript Decision

Para: Carlos Henrique Barrios Cc: Marcio Debiasi, Tomás

I am pleased to inform you that your manuscript, "Estimation of Premature Deaths due to Lack of Access to anti-HER2 therapy for Advanced Breast Cancer in the Brazilian Public Health System," has been accepted for publication in Journal of Global Oncology. See below for important information concerning proofs, National Institutes of Health grantees (if applicable), and embargo.

# Clinical Protocol / Guideline

- Cancer is a global Epidemic
- Effective treatments, but complex and confuse evidence
- Judicialization
- **Results in Brazil are not good: need for local guides**

# Cancer Mortality

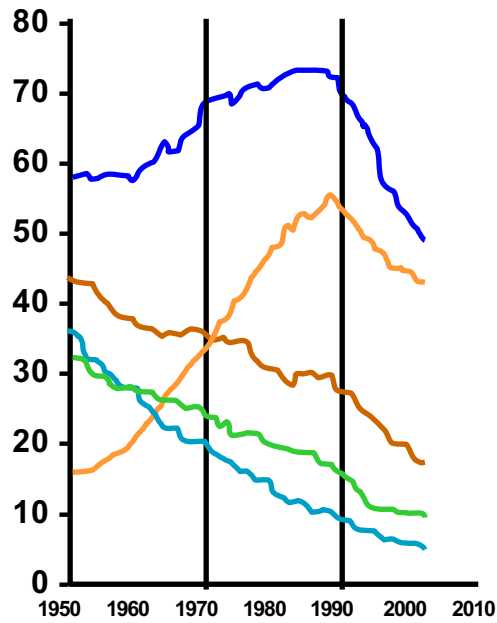
Reduction since 1990

-33%

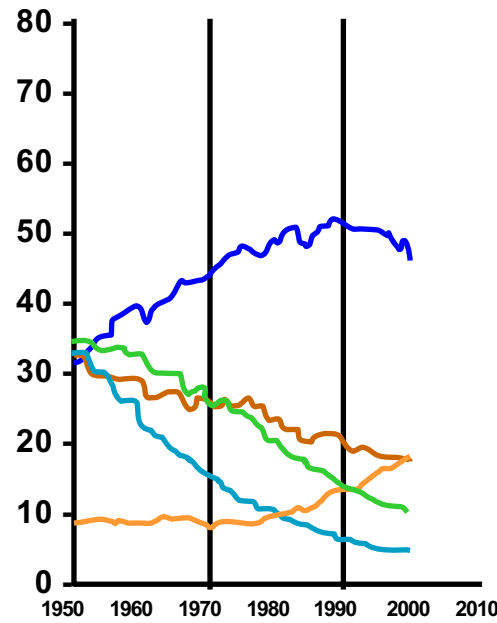
-10%

-25%

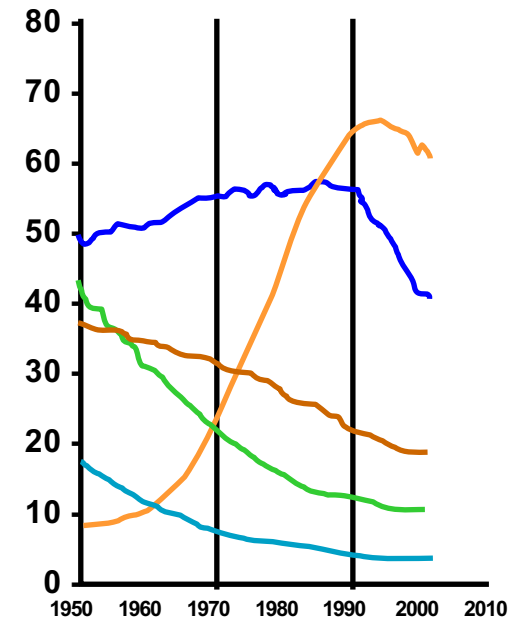
Annual mortality per  
100,000 women age 35-69



UK



France

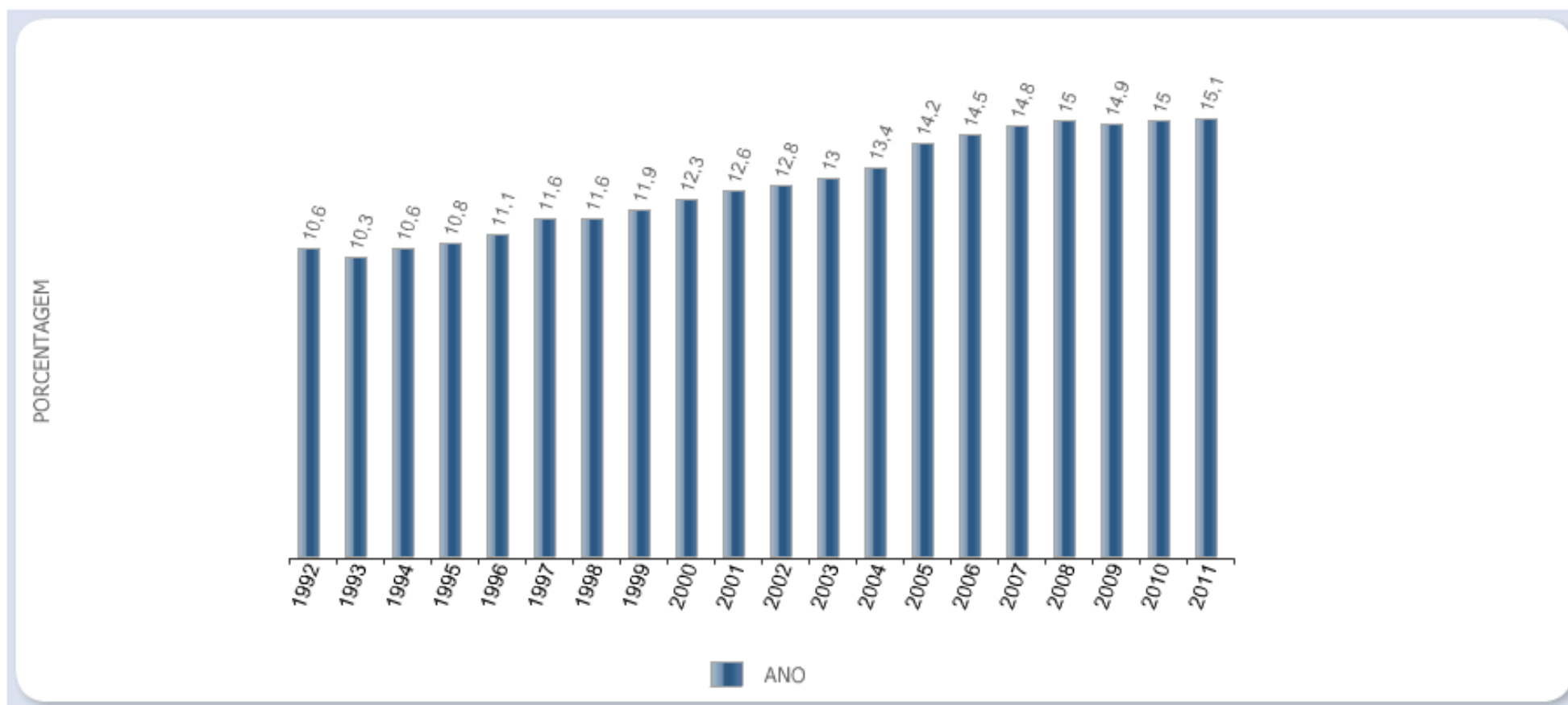


USA

■ Breast ■ Lung ■ Colorectal ■ Uterus ■ Gastric

# CÂNCER NO BR: MORTALIDADE

Mortalidade proporcional não ajustada por câncer, Brasil, homens e mulheres, entre 1992 e 2011.



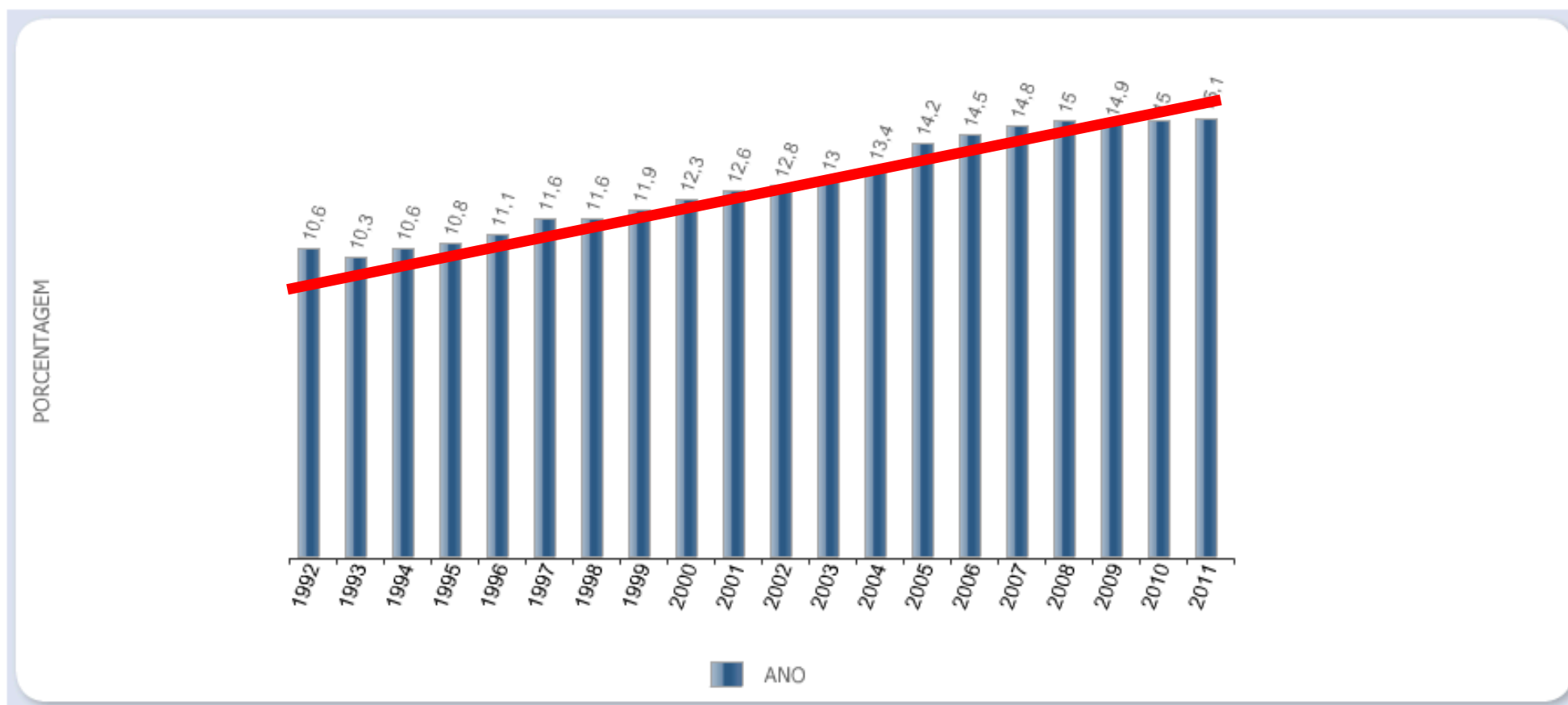
Fontes: MS/SVS/DASIS/CGIAE/Sistema de Informação sobre Mortalidade - SIM  
MP/Fundação Instituto Brasileiro de Geografia e Estatística - IBGE  
MS/INCA/CGPV/Divisão de Vigilância e Análise de Situação.

INCA, 2014



# CÂNCER NO BR: MORTALIDADE

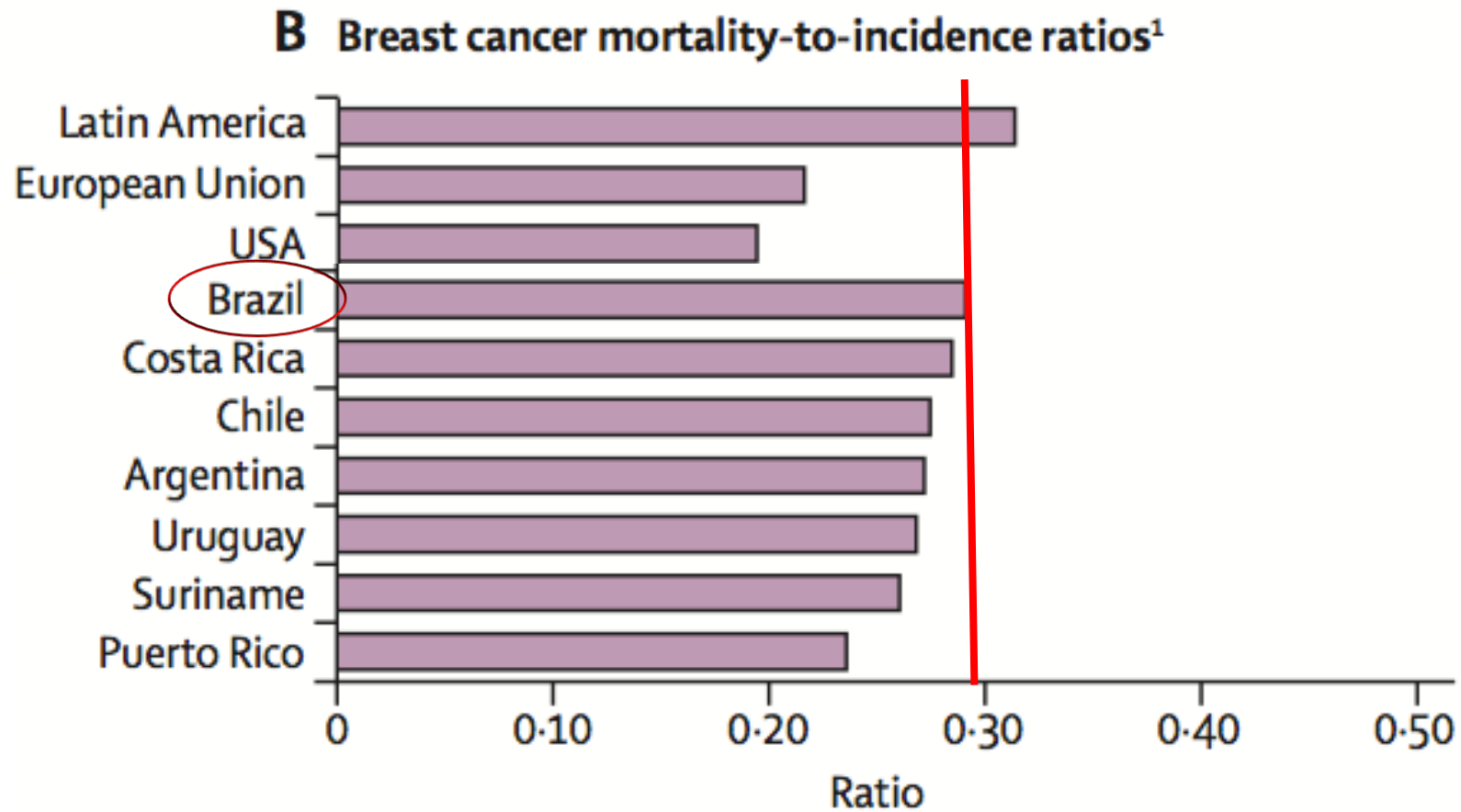
Mortalidade proporcional não ajustada por câncer, Brasil, homens e mulheres, entre 1992 e 2011.



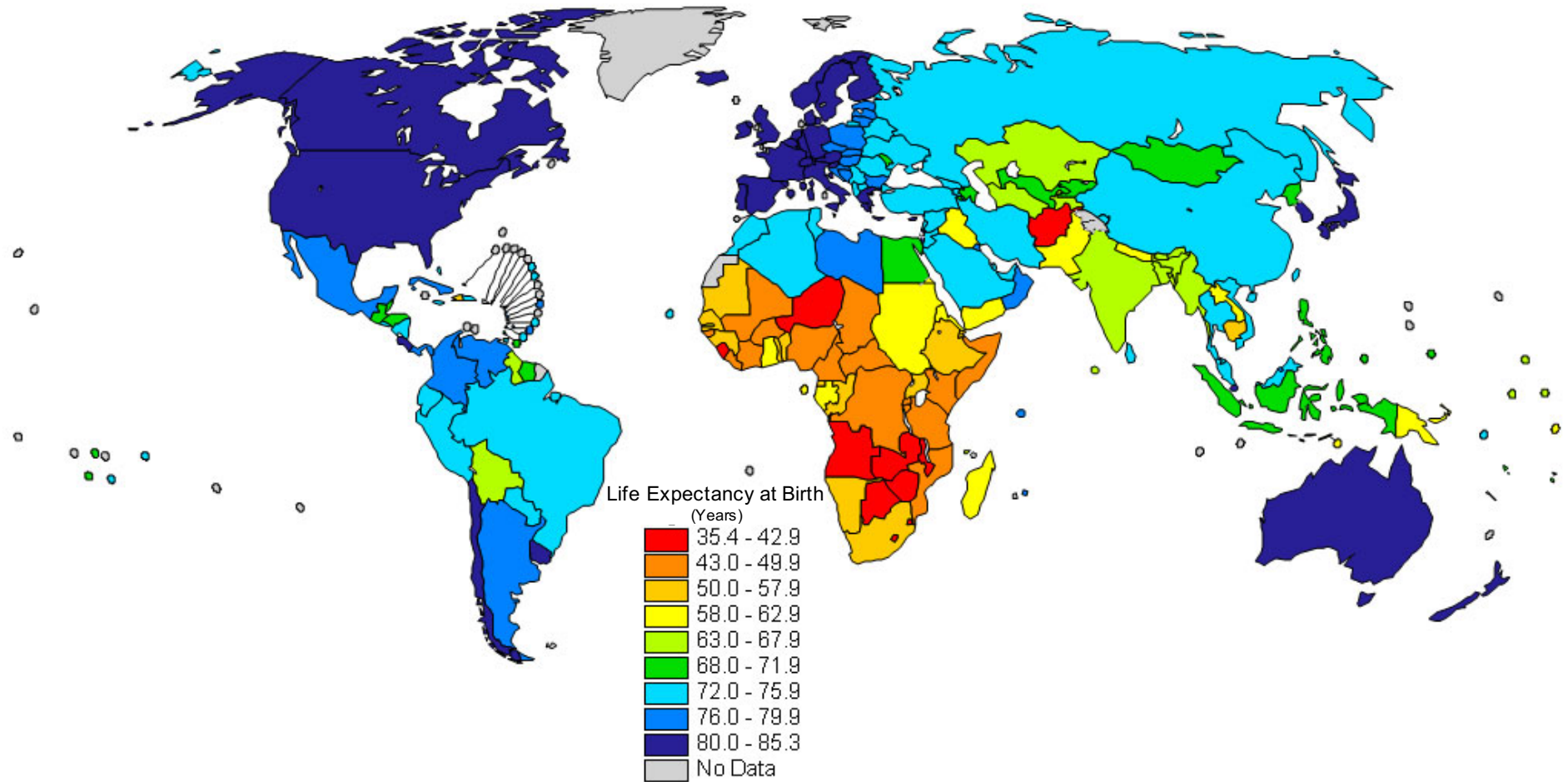
Fontes: MS/SVS/DASIS/CGIAE/Sistema de Informação sobre Mortalidade - SIM  
MP/Fundação Instituto Brasileiro de Geografia e Estatística - IBGE  
MS/INCA/CGPV/Divisão de Vigilância e Análise de Situação.

INCA, 2014

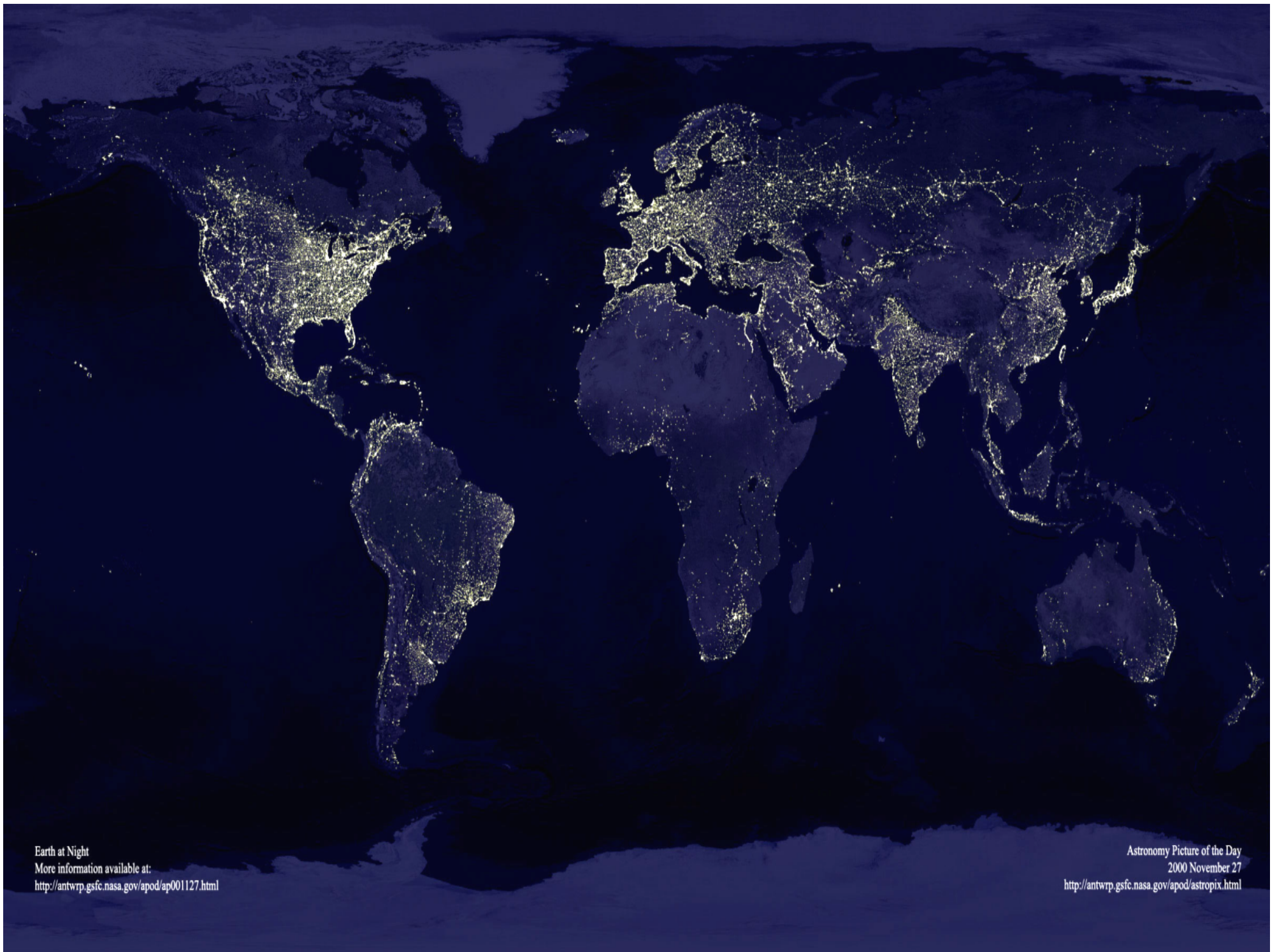
# DIAGNÓSTICO PRECOCE: importância



# Life Expectancy World Map



Source: UN Population Division, 2006.



Earth at Night  
More information available at:  
<http://antwrp.gsfc.nasa.gov/apod/ap001127.html>

Astronomy Picture of the Day  
2000 November 27  
<http://antwrp.gsfc.nasa.gov/apod/astropix.html>

---

# Clinical Protocol / Guideline

# HOW?

---

# Clinical Protocol / Guideline

- ▣ Systematic review of the literature

---

# LOOKING AT THE EVIDENCE



**PubMed.gov**

US National Library of Medicine  
National Institutes of Health



When you look at the evidence

...





... you gotta look at it thoroughly



# Clinical Protocol / Guideline

- ▣ Systematic review of the literature
  - ▣ Databases: PubMed, Embase, Cochrane, Lilacs
  - ...
  - ▣ Medical Societys and other Guidelines
  - ▣ Specialists` opinions
  - ▣ Research question:
    - ▣ P: patient
    - ▣ I: intervention
    - ▣ C: comparison
    - ▣ O: outcome

# Clinical Protocol / Guideline

- Systematic review of the literature
- WHO??
  - Medical Society
  - National Agency
  - Government

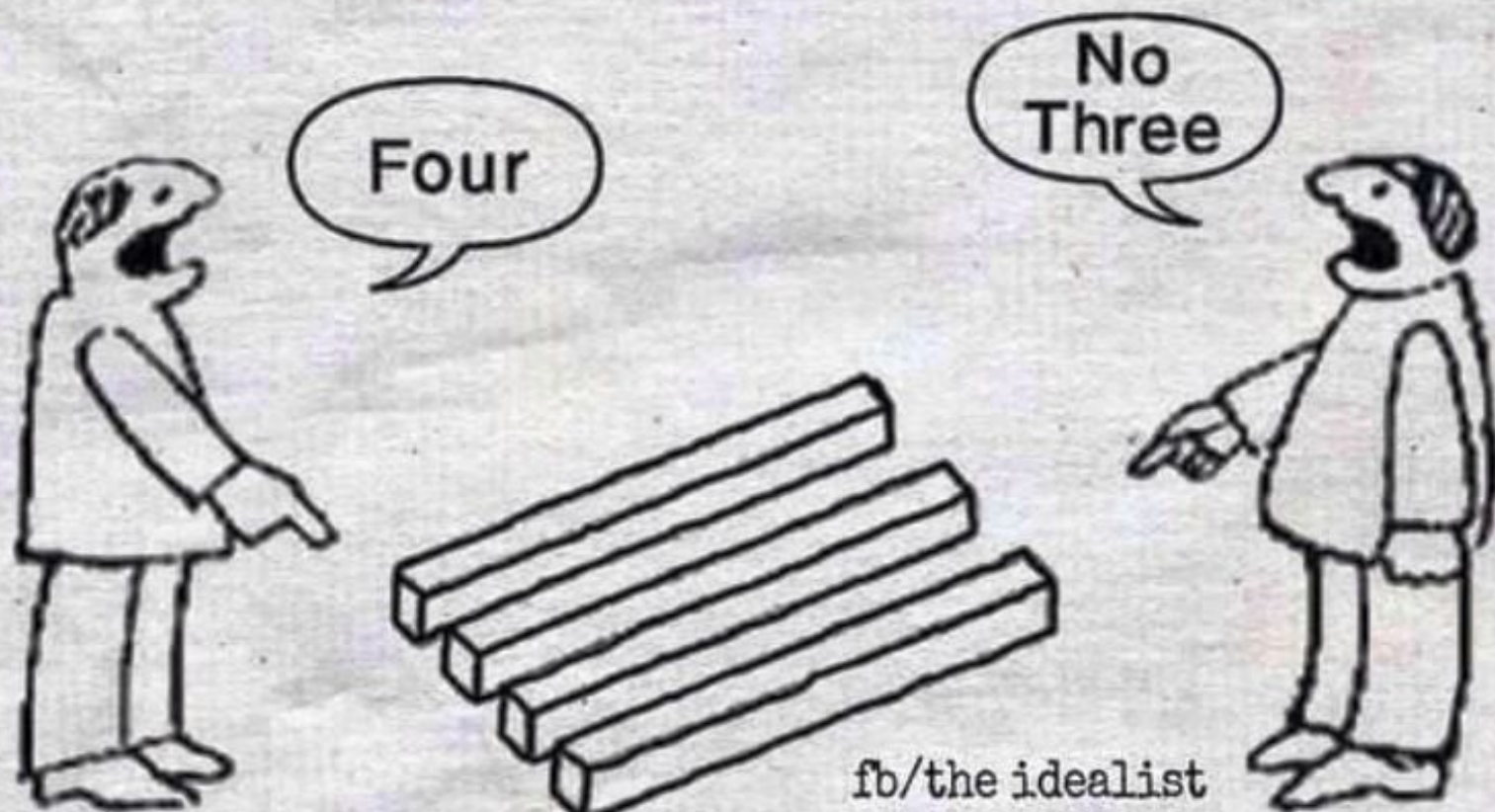


# Clinical Protocol / Guideline

- **Systematic review of the literature**
- **WHO??**
- **Structure**
  - **Introduction:** state the clinical problem and the state of art knowledge
  - **Methods**
  - **Results:** text and table summaries
  - **Conclusions:** have to be CLINICALLY MEANINGFULL

**"Everything we hear  
is an opinion, not a fact.  
Everything we see  
is a perspective, not the truth."**

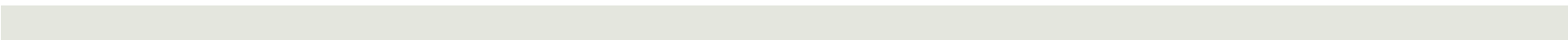
- Marcus Aurelius



---

**Be careful**

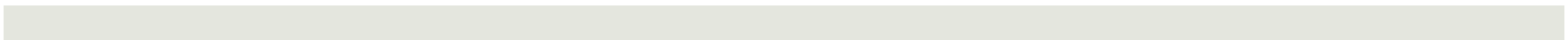
...



# SWANS ...



# CAN LOOK LIKE ELEPHANTS!!!







Swans Reflecting Elephants (1937) – Salvador Dalí



**LACOG**  
LATIN AMERICAN  
COOPERATIVE  
ONCOLOGY GROUP

**OBRIGADO**

---



**LACOG**

LATIN AMERICAN  
COOPERATIVE  
ONCOLOGY GROUP

**Márcio Debiasi**

Scientific Director

LACOG Coordinating Office

[marcio.debiasi@lacog.org.br](mailto:marcio.debiasi@lacog.org.br)

---