

# Estudos observacionais

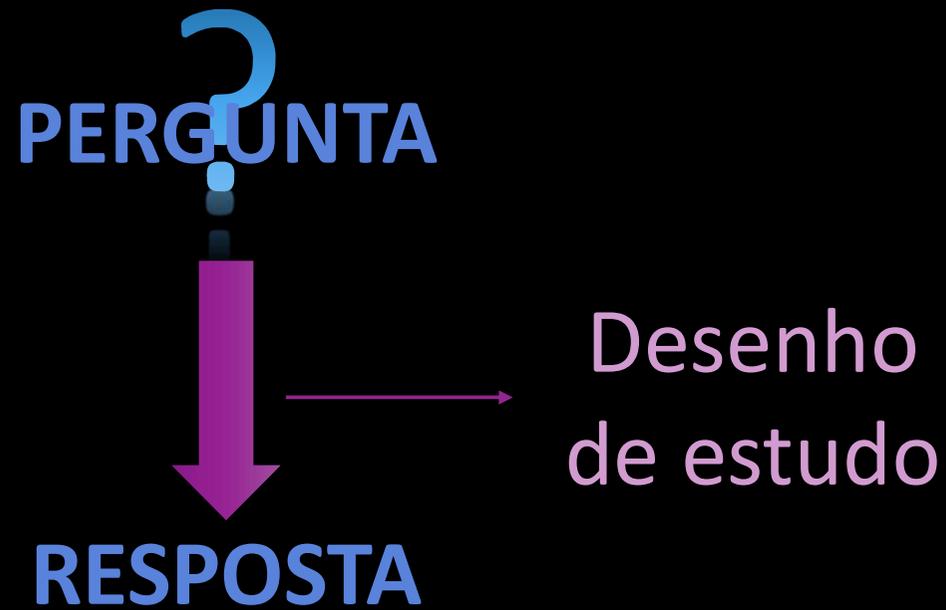
MFT 5725 – Pesquisa clínica: delineamento, e  
condução, processamento de sinais biológicos e  
tratamento estatístico

Programa de Ciências da Reabilitação

Profa. Dra. Eneida Yuri Suda



# PESQUISA



# Tipos de pesquisa

- Pesquisas descritivas
- Pesquisas com hipótese
  - Testam hipótese de associação
  - Testam hipótese de causa e efeito

Toda pesquisa pode ter hipótese, mas nem toda pesquisa requer hipótese

Resposta a uma pergunta, mas que ainda não foi testada

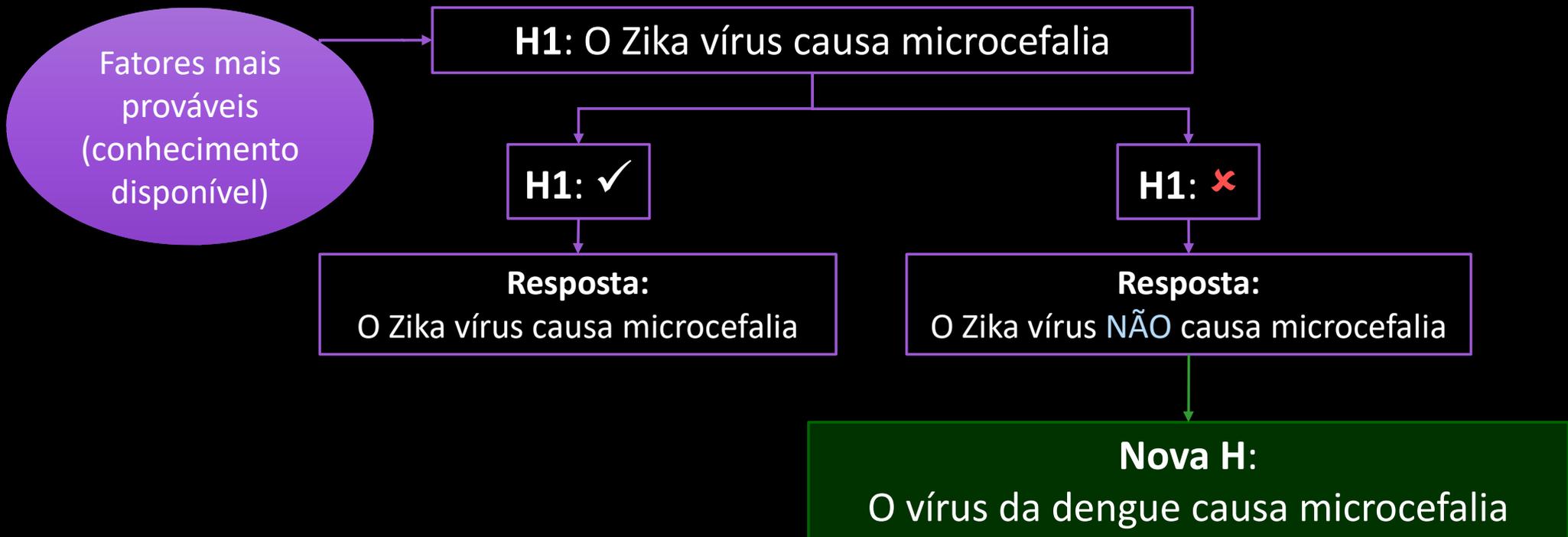
Possibilidade de resposta

# Tipos de pesquisa

**Pergunta:**

Quais fatores causam microcefalia em crianças?

PERGUNTA  
↓  
RESPOSTA



# Tipos de pesquisa

## Pergunta:

Qual o percentual de crianças brasileiras com microcefalia, cujas mães foram infectadas com o Zika vírus na gestação?

~~H1~~: 55,0% das crianças desenvolvem microcefalia

~~H2~~: 40,3% das crianças desenvolvem microcefalia

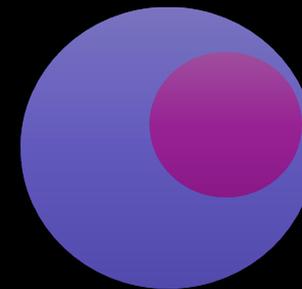
~~H3~~: 70,8% das crianças desenvolvem microcefalia

...

PERGUNTA



RESPOSTA



% Indivíduos que desenvolveram a condição

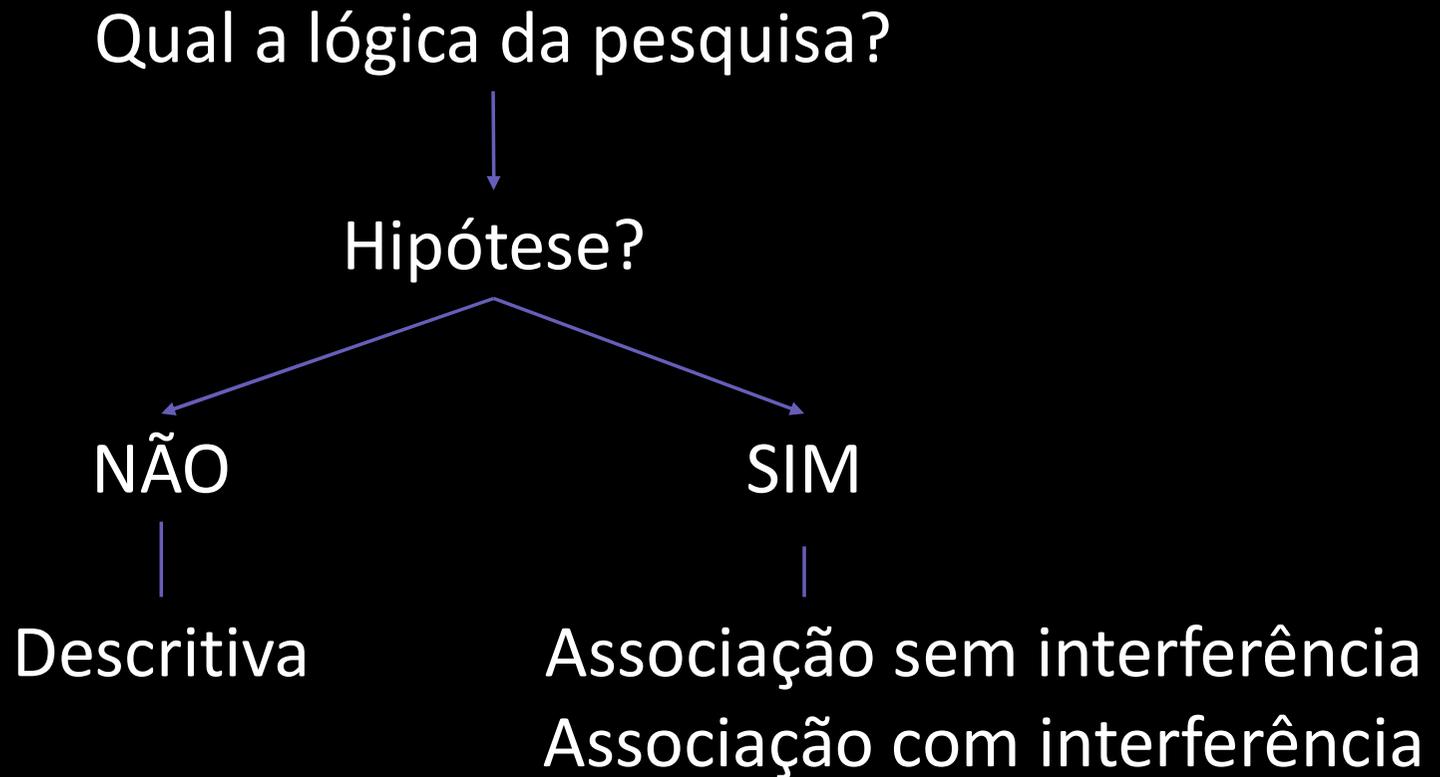
Resposta:

60,1% das crianças desenvolvem microcefalia

Nova H?



# Tipos de pesquisa



# Tipos de pesquisa

## Pesquisas com HIPÓTESE

- Testam a relação entre duas ou mais variáveis

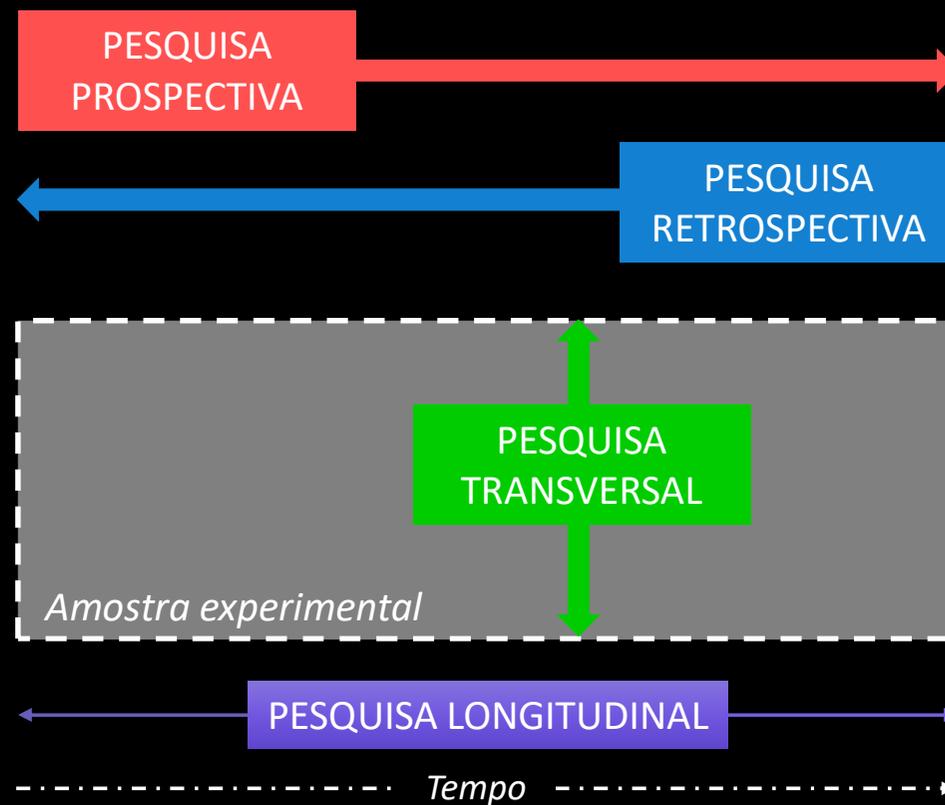
→ Associação - Fator externo

→ Interferência - Causa e efeito (interferência)



Mecanismo

# Desenhos de estudo



# Desenhos de estudo

- **Estudos longitudinais** - medidas repetidas em intervalos regulares no mesmo sujeito
  - Estabelece a sequência correta dos eventos
  - Dificuldade na logística - motivação, transporte, , lembrar data teste
  - Perda amostra, custo operacional alto
- **Estudos transversais** – sujeito observado uma vez.
  - Mais fácil condução.
  - Representatividade amostra, representação relativa ao momento da coleta, mascara variação individual

# Desenhos de estudo



- Estudos observacionais - sem intervenção.
  - Retrospectivo - observa um efeito e busca retrospectivamente a causa
  - Prospectivo - observa-se uma amostra na qual a causa já possa ter ocorrido, mas os efeitos ainda não.



- Estudos experimentais – randomização, controle e intervenção.
  - Prospectivo

# Pesquisas descritivas

Qual a lógica da pesquisa?



Hipótese?



# Pesquisas descritivas



- Visam exclusivamente descrever variáveis
  - Ex: uma certa estrutura, a prevalência de certa doença, um comportamento, uma resposta bioquímica, física, fisiológica, farmacológica, etc...
- Não há qualquer referência à causa ou associação com outras variáveis

# Estudos descritivos



## 1. Relato de caso e séries de casos

- Descrição de um único sujeito (relato de caso) ou um pequeno grupo de sujeitos (série de casos)
- Doenças novas ou efeitos devido à exposição a algum agente
- Doenças muito raras
- Não há um de grupo controle
- Rápidos e de baixo custo

*Lancet Infect Dis.* 2017 May;17(5):520-527. doi: 10.1016/S1473-3099(17)30102-0. Epub 2017 Feb 11.

## Analysis of blood from Zika virus-infected fetuses: a prospective case series.

Schaub B<sup>1</sup>, Vouga M<sup>2</sup>, Najjioullah F<sup>3</sup>, Gueneret M<sup>4</sup>, Monthieux A<sup>5</sup>, Harte C<sup>5</sup>, Muller F<sup>6</sup>, Jolivet E<sup>4</sup>, Adenet C<sup>7</sup>, Dreux S<sup>6</sup>, Leparac-Goffart I<sup>8</sup>, Cesaire R<sup>9</sup>, Volumenie JL<sup>4</sup>, Baud D<sup>10</sup>.

### ⊕ Author information

#### Abstract

**BACKGROUND:** Zika virus has spread through the Americas and the Caribbean since early 2015 and was rapidly declared a Public Health Emergency of International Concern by WHO because of the potential association with fetal anomalies. We analysed fetal and maternal fluids and tissues in fetuses with confirmed Zika virus infection prospectively monitored in Martinique, a French Caribbean island.

**METHODS:** Since the beginning of the Zika virus outbreak in Martinique, all pregnant women undergo monthly fetal ultrasound examination surveillance. In this study, we prospectively studied all patients with fetal anomalies and a positive amniotic fluid for Zika virus by RT-PCR. Maternal and fetal blood, urine, amniotic fluid, placenta, and fetal tissues were tested for Zika virus by RT-PCR. Fetal blood was analysed to identify haematological and biological anomalies.

**FINDINGS:** Between Jan 1, 2016, and Nov 10, 2016, we recruited eight cases of Zika virus infection. All but two cases were symptomatic during the first trimester. Fetal anomalies were only detected after 20 weeks' gestation. After an initial positive result, amniocentesis became negative in two cases and fetal blood was transiently Zika virus-positive in six cases. Fetal blood analyses showed a cholestatic pattern, anaemia, and infectious response.

**INTERPRETATION:** Normalisation of amniotic fluid and fetal blood for Zika virus, as well as maternal blood and urine, shows the limitations of the performance of these investigations, due to the possibility of false negative results. Abnormal fetal blood needs to be investigated further to establish prognostic factors of severe Zika virus infections.

*Prenat Diagn.* 2016 Sep;36(9):882-7. doi: 10.1002/pd.4882. Epub 2016 Aug 23.

## Associated ultrasonographic findings in fetuses with microcephaly because of suspected Zika virus (ZIKV) infection during pregnancy.

Carvalho FH<sup>1</sup>, Cordeiro KM<sup>1</sup>, Peixoto AB<sup>2,3</sup>, Tonni G<sup>4</sup>, Moron AF<sup>3</sup>, Feitosa FE<sup>1</sup>, Feitosa HN<sup>1</sup>, Araujo Júnior E<sup>5</sup>.

### ⊕ Author information

#### Abstract

**OBJECTIVE:** To describe fetal ultrasonographic findings and outcomes in a series of cases of fetal microcephaly associated with Zika virus infection.

**METHODS:** Retrospective case series of microcephaly with definite (laboratory evidence) or highly probable (specific neuroimaging findings and negative laboratory results) maternal Zika virus infection. Microcephaly was graded as mild if the head circumference was between 2 and 3 standard deviation (SD) below the mean, and severe if 3 or more SD below the mean. Associated central nervous system (CNS) and extracranial malformations are described.

**RESULTS:** Nineteen singleton pregnancies fulfilling the inclusion criteria were identified. Severe microcephaly and mild microcephaly were identified in 14 and 5 fetuses, respectively. Additional CNS malformations were present in 17 cases and 7 had extracranial congenital anomalies. Symptoms were reported in 13/19 cases at a gestational age between 5 and 16 weeks. Mean ( $\pm$ SD) gestational age at ultrasound diagnosis was  $32.3 \pm 5.1$  weeks. Amniocentesis was performed in five cases at a median gestational age of 31 weeks (range 28-38) and was positive for Zika virus RT-PCR in two cases. There were three neonatal deaths and one stillbirth.

**CONCLUSION:** In the presence of fetal microcephaly associated with Zika virus infection, CNS malformations are frequently detected. © 2016 John Wiley & Sons, Ltd.

# Estudos descritivos



## 2. Transversal

- Descrição de um certo resultado ou efeito e uma fonte de exposição, que são medidos simultaneamente
- Fornece uma “foto instantânea” das características e da frequência de um determinado resultado em um dado instante

# Estudos descritivos

## 2. Transversal ...

- Efeitos de causa e efeito **não** podem ser determinadas
  - Não há como determinar se a exposição ocorreu antes ou após o desfecho
- Mede a **prevalência** de doenças
- Útil para gerar hipóteses e planejar ações de saúde

**Prevalência** = proporção de pessoas que apresentam a doença em um determinado momento



Neurol Int. 2018 Jul 4;10(2):7638. doi: 10.4081/ni.2018.7638. eCollection 2018 May 24.

## Prevalence of neurological complications associated with Zika virus in a Brazilian metropolis.

Brito KGDS<sup>1</sup>, Dos Santos EB<sup>1</sup>, Lucas LDSM<sup>1</sup>, Orsini M<sup>2,3</sup>, Fiorelli R<sup>2</sup>, Teixeira S<sup>4</sup>, Ayres C<sup>4</sup>, Correia L<sup>4</sup>, Bastos VH<sup>4</sup>, Trajano E<sup>2</sup>, Cardoso CE<sup>2</sup>, de Freitas MRG<sup>5</sup>, Catharino AMDS<sup>1,6</sup>.

### + Author information

### Abstract

The aim of this paper is to study the prevalence of Zika Virus (ZIKV) and the index of its neurological complications. This is a quantitative, cross-sectional epidemiological study. Data were collected through the compulsory notification of suspected ZIKV and its neurological alterations cases. 113 suspected ZIKV cases were reported, most of them in the summer, with a higher prevalence of females and in the fourth decade of life. Among the neurological changes, 15 Guillain-Barré Syndrome cases were reported, with one registered death. As neurological manifestations, most of them started 30 days after a ZIKV infection. No case has been confirmed laboratory. It is necessary to combat the vector, mainly in the summer, to reduce ZIKV infection and its neurological complications, besides instruction to the health professionals about these complications and serological tests requests for an accurate diagnosis.

**KEYWORDS:** Guillain-Barré; Zika virus; infection; microcephaly; syndrome

*Int J Environ Res Public Health*. 2018 May 29;15(6). pii: E1107. doi: 10.3390/ijerph15061107.

## Functioning and Disability Profile of Children with Microcephaly Associated with Congenital Zika Virus Infection.

Ferreira HNC<sup>1</sup>, Schiariti V<sup>2</sup>, Regalado ICR<sup>3</sup>, Sousa KG<sup>4</sup>, Pereira SA<sup>5</sup>, Fechine CPNDS<sup>6</sup>, Longo E<sup>7</sup>.

### ⊕ Author information

#### Abstract

**INTRODUCTION:** The increase in the number of cases of microcephaly in Brazil and its association with the Zika virus (ZIKV) is a global public health problem. The International Classification of Functioning Disability and Health (ICF) model is a powerful tool and extremely relevant in managing disability.

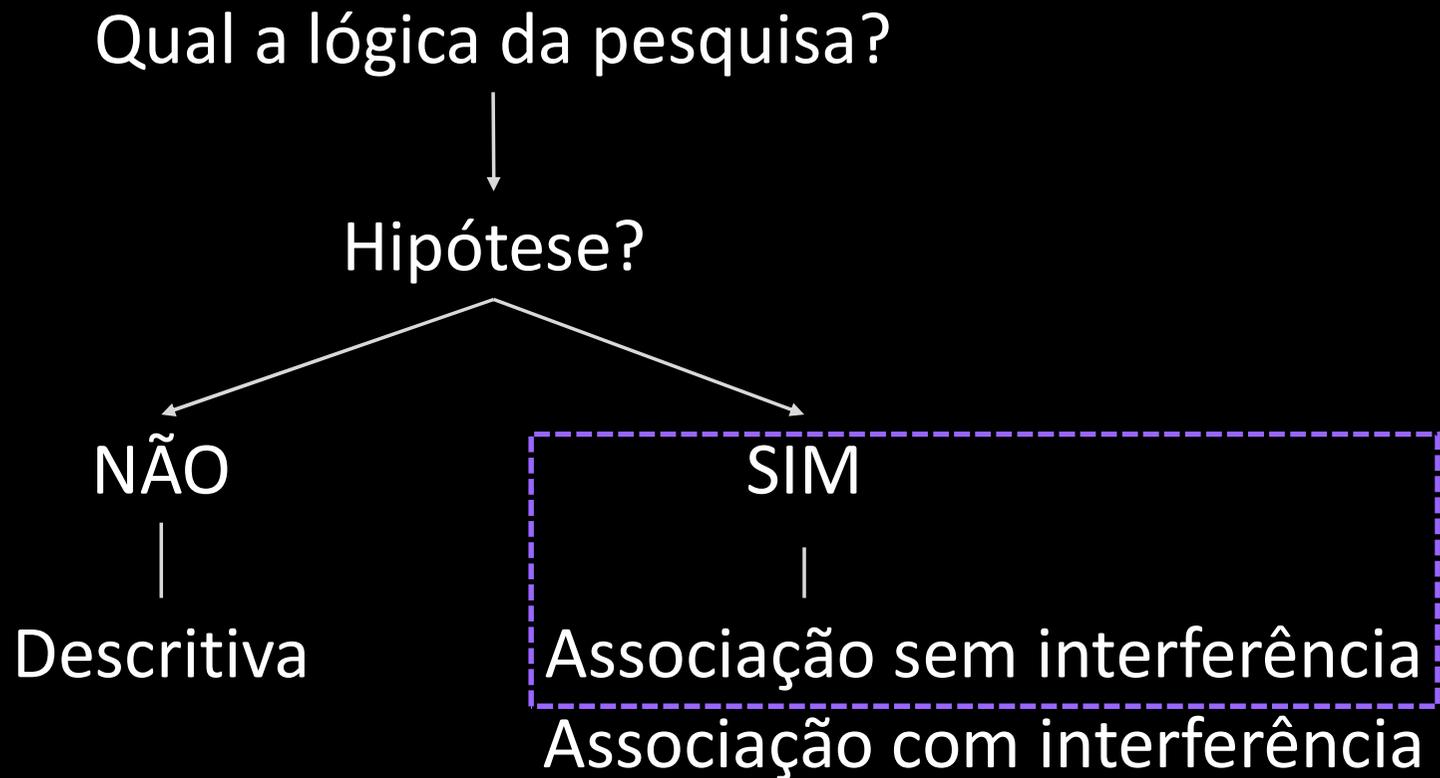
**OBJECTIVE:** Describe the functioning profile of children with microcephaly associated with ZIKV in two states of northeastern Brazil.

**METHODS:** This is a **descriptive cross-sectional** study. The sociodemographic characteristics, head circumference, and other clinical data were collected from medical charts, physical examinations, measuring instruments, and interviews with the children and their parents. The Brazilian Portuguese version of the Brief Common ICF Core Set for cerebral palsy (CP) was used. Each ICF category was assigned a qualifier, which ranged from 0 to 4 (no problem, mild problem, moderate problem, severe problem, complete problem). For environmental factors, 0 represents no barrier and 4 represents complete barrier; +0, no facilitator and +4, complete facilitator.

**RESULTS:** A total of 34 children with microcephaly caused by ZIKV were recruited (18 girls and 16 boys) at four rehabilitation facilities in Rio Grande do Norte and Paraíba states, Brazil. The average age of the participants was 21 months, monthly income was ≈USD 300.00, and head circumference z-scores ranged between 0.92 and -5.51. The functioning profile revealed complete disability in most of the body function categories (b). The activity and participation areas (d) were highly impacted, particularly in mobility-related categories. With respect to environmental factors (e), most of the sample reported a complete facilitator for the immediate family, friends, and health services, systems, and policies, as well as a complete barrier to societal attitudes.

**CONCLUSION:** This is the first study that describes the functioning profile of children with microcephaly associated with ZIKV, using a tool based on the ICF in Brazil. Our findings reinforce the need to maximize health care and access to information, based on the ICF, for multiprofessional teams, administrators, family members, and children.

# Pesquisas observacionais analíticas



# Pesquisas de associação entre variáveis

- Testa-se se duas ou mais variáveis estão **associadas** entre si
- Associação **sem relação causal**
  - Ex: identificar que a microcefalia ocorre com maior incidência em crianças cujas mães foram expostas ao Zika vírus não significa que o vírus foi o causador da condição
- Caracterização de relações que **não são** modificadas

# Estudos observacionais analíticos



- Identificam: Etiologia  
Fatores de risco  
Fatores prognósticos
1. Estudos coorte
  2. Estudos caso-controle
  3. Revisão sistemática e metanálise

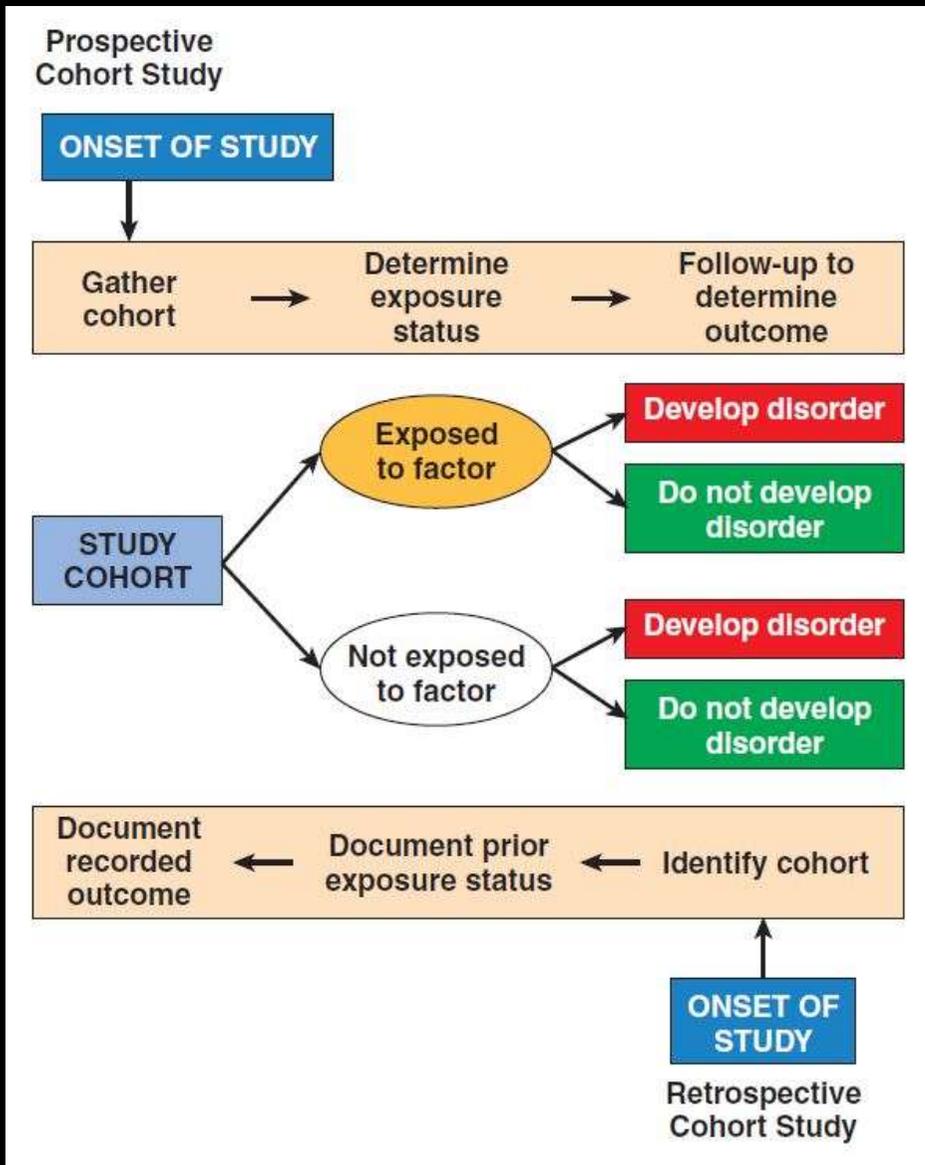
## Estudo de Coorte

- OBJ: Determinar quais fatores estão associados ao desenvolvimento de um desfecho
- **Coorte** = Grupo de indivíduos com alguma característica em comum, seguido ao longo do tempo
- Nenhum indivíduo pode apresentar no início do seguimento o evento que se quer estudar
- Todos os indivíduos têm que ser suscetíveis à ocorrência do evento

### Desvantagens:

- Seguimento prolongado
- Demorados e de alto custo

Prospectivo



**Incidência** = eventos novos que surgem em uma população em um período de tempo

**Risco** = 
$$\frac{n \text{ pessoas que ficaram doentes no período}}{n \text{ pessoas na pop no início sem doença}}$$



## Effect of acute Zika virus infection on sperm and virus clearance in body fluids: a prospective observational study

Guillaume Joquet, Jean-Michel Mansuy, Giulia Matusali, Safouane Hamdi, Marie Walschaerts, Lynda Pavili, Stefanie Guyomard, Nadia Prisant, Pierre Lamarre, Nathalie Dejuca-Rainsford, Christophe Pasquier, Louis Bujan

### Summary

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17: 1200–08

Published Online  
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[http://dx.doi.org/10.1016/S1473-3099\(17\)30444-9](http://dx.doi.org/10.1016/S1473-3099(17)30444-9)

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Centre Caribéen de Médecine de la Reproduction (CCMR) CECOS CARAIBES, CHU de Pointe-à-Pitre, Pointe-à-Pitre, Guadeloupe, France (G Joquet MD, N Prisant MD, L Pavili PharmD); Laboratoire de Virologie, Institut Fédératif de Biologie (J-M Mansuy PhD, Prof C Pasquier PhD), Département de Biochimie et d'Hormonologie, Institut Fédératif de Biologie (S Hamdi PhD), Research Group on Human Fertility EA 3694, University Paul Sabatier Toulouse III—CECOS, Hôpital Paule de Viguier (M Walschaerts PhD, S Hamdi, Prof L Bujan PhD), CHU Toulouse, Toulouse, France; Institut National de la Santé et de la Recherche Médicale (Inserm), Institut de Recherche en Santé, Environnement et Travail (Irset-Inserm UMR 1085), Structure Fédérative de Recherche Biosit, UMS CNRS 3480/US Inserm 018, Rennes,

**Background** Evidence of human sexual transmission during Zika virus emergence is a matter of concern, particularly in procreation, but to date, kinetics of seminal shedding and the effects of infection on human reproductive function have not been described. To investigate the effects of Zika virus infection on semen and clearance of Zika virus from semen and body fluids, we aimed to study a cohort of Zika virus-infected men

**Methods** This prospective observational study recruited men presenting with acute Zika virus infection at Pointe-à-Pitre University Hospital in Guadeloupe, French Caribbean, where a Zika virus outbreak occurred between April and November, 2016. Blood, urine, and semen were collected at days 7, 11, 20, 30, 60, 90, and 120 after symptom onset, and semen characteristics, such as total sperm count, sperm motility, vitality, and morphology, and reproductive hormone concentrations, such as testosterone, inhibin, follicle-stimulating hormone, and luteinising hormone, were assessed. At days 7, 11, and 20, semen was processed to isolate motile spermatozoa. Zika virus RNA was detected by RT-PCR using whole blood, serum, urine, seminal plasma, semen cells, and motile spermatozoa fractions. Zika virus was isolated from different sperm fractions on Vero E6 cultures.

**Findings** 15 male volunteers (mean age 35 years [SD 5; range 25–44] with acute Zika virus infection and positive Zika virus RNA detection in blood or urine were enrolled. Total sperm count was decreased from median  $119 \times 10^6$  spermatozoa (IQR 22–234) at day 7 to  $45 \cdot 2 \times 10^6$  ( $16 \cdot 5$ – $89 \cdot 6$ ) at day 30 and  $70 \times 10^6$  ( $28 \cdot 5$ – $81 \cdot 4$ ) at day 60, respectively, after Zika virus infection. Inhibin values increased from  $93 \cdot 5$  pg/mL (IQR 55–162) at day 7 to  $150$  pg/mL (78–209) at day 120 when total sperm count recovered. In motile spermatozoa obtained after density gradient separation, Zika virus RNA was found in three of 14 patients at day 7, four of 15 at day 11, and four of 15 at day 20 and replication-competent virus was found in the tested patient. Seminal shedding kinetics seemed heterogeneous among patients. Whole blood was the fluid most frequently positive for Zika virus RNA (62 of 92 samples) and three patients remained positive at day 120.

**Interpretation** Semen alterations early after acute Zika virus infection might affect fertility and could be explained by virus effects on the testis and epididymis. Frequency of shedding and high viral load in semen, together with the presence of replicative virus in a motile spermatozoa fraction, can lead to Zika virus transmission during sexual contact and assisted reproduction procedures. Whole blood seems to be the best specimen for Zika virus RNA detection, diagnosis, and follow-up.

Obstet Gynecol. 2018 Aug;132(2):487-495. doi: 10.1097/AOG.0000000000002737.

## Zika Virus Infection Among Pregnant Women and Their Neonates in New York City, January 2016-June 2017.

Conners EE<sup>1</sup>, Lee EH, Thompson CN, McGibbon E, Rakeman JL, Iwamoto M, Cooper H, Vora NM, Limberger RJ, Fine AD, Liu D, Slavinski S; Zika Working Group.

### ⊕ Author information

### Abstract

**OBJECTIVE:** To describe and compare differences in the epidemiologic, clinical, and laboratory characteristics of pregnant women with confirmed or probable Zika virus infection and to compare the risk of having a neonate with laboratory evidence of Zika virus infection with that of having a neonate without evidence of Zika virus infection by maternal characteristics.

**METHODS:** We conducted a retrospective cohort study of women with Zika virus infection who completed pregnancy in New York City from January 1, 2016 to June 30, 2017. Confirmed Zika virus infection was defined as 1) nucleic acid amplification test-detected Zika virus, or 2) a nonnegative enzyme-linked immunosorbent assay test result and a plaque-reduction neutralization test result positive for Zika virus but negative for dengue virus, or 3) delivery of a neonate with laboratory evidence of Zika virus infection. Probable infection was defined as a nonnegative enzyme-linked immunosorbent assay test result and a positive plaque-reduction neutralization test result for Zika virus and dengue virus.

**RESULTS:** We identified 390 women with confirmed (28%) or probable (72%) Zika virus infection. Fever, rash, arthralgia, or conjunctivitis was reported by 31% of women and were more common among women with confirmed than with probable infection (43% vs 26%,  $P=.001$ ). Of 366 neonates born to these women, 295 (81%) were tested for Zika virus and 22 (7%) had laboratory-diagnosed congenital Zika virus infection. The relative risk (RR) for having a neonate with laboratory evidence of Zika virus infection was greater among women with fever (RR 4.8, 95% CI 2.1-10.7), tingling (RR 4.8, CI 1.7-13.7), or numbness (RR 6.9, CI 2.6-18.2) during pregnancy or the periconception period. However, the RR did not differ whether the mother had confirmed or probable Zika virus infection (RR 1.6, CI 0.7-4.1).

**CONCLUSION:** In New York City, a greater proportion of women had probable Zika virus infection than confirmed infection. Women with some symptoms during pregnancy or periconceptionally were more likely to have a neonate with laboratory evidence of Zika virus infection. Neonates born to women with confirmed or probable Zika virus infection should be tested for Zika virus infection.

## Estudo de Caso-Controle

- OBJ: identificar quais fatores podem contribuir para o desenvolvimento de um desfecho
- Comparação entre dois grupos de uma mesma população: doentes (**caso**) x saudáveis (**controle**)
- **Restrospectivo**: Exposição ou não ao fator
- Grupos homogêneos e indivíduos suscetíveis à doença



# Estudo de Caso-Control

- Doenças de baixa incidência (raras) ou com período de latência longo
- Alternativa mais rápida e barata ao estudo de coorte



## Desvantagens:

- Viés de memória

Pessoas que apresentam a doença em um estudo tendem a lembrar-se mais da exposição a um eventual fator de risco, mesmo que na realidade não tenham sido expostas



# Association between microcephaly, Zika virus infection, and other risk factors in Brazil: final report of a case-control study

ESTUDOS OBSERVACIONAIS  
ANALÍTICOS

Thália Velho Barreto de Araújo, Ricardo Arraes de Alencar Ximenes, Demócrito de Barros Miranda-Filho, Wayner Vieira Souza, Ulisses Ramos Montarroyos, Ana Paula Lopes de Melo, Sandra Valongueiro, Maria de Fátima Pessoa Militão de Albuquerque, Cynthia Braga, Sinval Pinto Brandão Filho, Marli Tenório Cordeiro, Enrique Vazquez, Danielle di Cavalcanti Souza Cruz, Claudio Maierovitch Pessanha Henriques, Luciana Caroline Albuquerque Bezerra, Priscila Mayrelle da Silva Castanha, Rafael Dhalia, Ernesto Torres Azevedo Marques-Júnior, Celina Maria Turchi Martelli\*, Laura Cunha Rodrigues\*, on behalf of investigators from the Microcephaly Epidemic Research Group, the Brazilian Ministry of Health, the Pan American Health Organization, Instituto de Medicina Integral Professor Fernando Figueira, and the State Health Department of Pernambuco†

## Summary

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This online publication has been corrected. The corrected version first appeared at [thelancet.com/infection](http://thelancet.com/infection) on January 4, 2018

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\*Contributed equally

†Investigators contributing on behalf of these organisations are listed in the appendix

Department of Social Medicine (TV B Araújo PhD, S Valongueiro PhD) and Department of Tropical Medicine

(Prof R A A Ximenes PhD), Federal University of Pernambuco, Recife, Brazil; University of Pernambuco, Recife, Brazil

(Prof R A A Ximenes, D B Miranda-Filho PhD, U R Montarroyos PhD); The Research Centre Aggeu Magalhães (CPqAM), Oswaldo Cruz Foundation (Fiocruz), Recife, Brazil (W V Souza PhD, M F R M Albuquerque PhD)

**Background** A Zika virus epidemic emerged in northeast Brazil in 2015 and was followed by a striking increase in congenital microcephaly cases, triggering a declaration of an international public health emergency. This is the final report of the first case-control study evaluating the potential causes of microcephaly: congenital Zika virus infection, vaccines, and larvicides. The published preliminary report suggested a strong association between microcephaly and congenital Zika virus infection.

**Methods** We did a case-control study in eight public maternity hospitals in Recife, Brazil. Cases were neonates born with microcephaly, defined as a head circumference of 2 SD below the mean. Two controls without microcephaly were matched to each case by expected date of delivery and area of residence. We tested the serum of cases and controls and the CSF of cases for detection of Zika virus genomes with quantitative RT-PCR and for detection of IgM antibodies with capture-IgM ELISA. We also tested maternal serum with plaque reduction neutralisation assays for Zika and dengue viruses. We estimated matched crude and adjusted odds ratios with exact conditional logistic regression to determine the association between microcephaly and Zika virus infection.

**Findings** We screened neonates born between Jan 15 and Nov 30, 2016, and prospectively recruited 91 cases and 173 controls. In 32 (35%) cases, congenital Zika virus infection was confirmed by laboratory tests and no controls had confirmed Zika virus infections. 69 (83%) of 83 cases with known birthweight were small for gestational age, compared with eight (5%) of 173 controls. The overall matched odds ratio was 73·1 (95% CI 13·0–∞) for microcephaly and Zika virus infection after adjustments. Neither vaccination during pregnancy or use of the larvicide pyriproxyfen was associated with microcephaly. Results of laboratory tests for Zika virus and brain imaging results were available for 79 (87%) cases; within these cases, ten were positive for Zika virus and had cerebral abnormalities, 13 were positive for Zika infection but had no cerebral abnormalities, and 11 were negative for Zika virus but had cerebral abnormalities.

**Interpretation** The association between microcephaly and congenital Zika virus infection was confirmed. We provide evidence of the absence of an effect of other potential factors, such as exposure to pyriproxyfen or vaccines (tetanus, diphtheria, and acellular pertussis, measles and rubella, or measles, mumps, and rubella) during pregnancy, confirming the findings of an ecological study of pyriproxyfen in Pernambuco and previous studies on the safety of Tdap vaccine administration during pregnancy.

# Revisão sistemática



- Reúne, de forma **organizada**, grande quantidade de resultados de pesquisas clínicas e auxiliam na explicação de diferenças encontradas entre estudos primários que investigam a mesma questão.
- Tem como objetivo identificar e incluir todos os **ensaios clínicos** relevantes
- Os "sujeitos" da investigação (unidade de análise) são os estudos primários selecionados através de método **sistemático** e pré-definido

# Revisão sistemática

- Responde a uma pergunta específica
- Utiliza **métodos** e **estratégias** pré-determinados para limitar possíveis vieses e erros aleatórios
- Pode incluir uma **metanálise** = síntese estatística dos resultados provenientes dos estudos incluídos
- Base confiável para a tomada de decisões
  - Seleção da informação relevante sem viés
  - Útil para a prática clínica, políticas de saúde, estudos futuros (cálculo poder estatístico)



# Revisão sistemática

## Características-chave

- Objetivos estabelecidos de forma clara
- Critérios de elegibilidade definidos *a priori*
- Metodologia explícita e reprodutível
- Pesquisa sistemática
- Avaliação da validade dos estudos incluídos
- Síntese sistemática e apresentação dos resultados





Sexually acquired Zika virus: a systematic review

Introduction

Materials and methods

Search strategy

Study criteria

Data extraction

Aims

Risk-of-bias assessment

Results

Risk-of-bias assessment

Transmission of ZIKV through sexual intercourse

Shedding of ZIKV in genital fluids

ZIKV shedding in male genital tract

ZIKV shedding in female genital tract

Timing of ZIKV



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journal homepage: [www.clinicalmicrobiologyandinfection.com](http://www.clinicalmicrobiologyandinfection.com)

## Systematic Review

## Sexually acquired Zika virus: a systematic review

J. Moreira<sup>1,\*</sup>, T.M. Peixoto<sup>2</sup>, A.M. Siqueira<sup>1,4</sup>, C.C. Lamas<sup>1,2,3,4</sup><sup>1</sup> Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz (FIOCRUZ), Rio de Janeiro, Brazil<sup>2</sup> Universidade do Grande Rio (Unigranrio), Rio de Janeiro, Brazil<sup>3</sup> Unidade de pesquisa cardiovascular, Instituto Nacional de Cardiologia, Rio de Janeiro, Brazil

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## ABSTRACT

**Background:** Zika virus (ZIKV) is transmitted to humans primarily by *Aedes* mosquito bites. However, circumstantial evidence points to a sexual transmission route.

**Objectives:** To assess the sexually acquired ZIKV cases and to investigate the shedding of ZIKV in genital fluids.

**Data sources:** PubMed, Scopus, Pro-MED-mail and WHO ZIKV notification databases from inception to December 2016.

**Selection criteria:** Reports describing ZIKV acquisition through sex and studies reporting the detection or isolation of ZIKV in the genital fluids were included.

**Risk-of-bias assessment:** The risk of bias was assessed using the National Institute of Health Tool.

**Results:** Eighteen studies reporting on sex-acquired ZIKV and 21 describing the presence of ZIKV in genital fluids were included. The overall risk of bias was moderate. Sexual transmission was male–female (92.5%), female–male (3.7%) and male–male (3.7%). Modes of sexual transmission were unprotected vaginal (96.2%), oral (18.5%) and anal (7.4%) intercourse. The median time between onset of symptoms in the index partner and presumed sexual transmission was 13 days (range 4–44 days). ZIKV RNA was detected in semen as late as 188 days (range 3–188 days) following symptom onset, and infectious virus was isolated in semen up to 69 days after symptom onset. No study reported ZIKV isolation from female genital samples, but detection did occur up to 13 days after symptom onset.

**Conclusions:** ZIKV is potentially sexually transmitted and persists in male genital secretions for a prolonged period after symptom onset.

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# Metanálise



- Método estatístico aplicado à revisão sistemática que integra os resultados de dois ou mais estudos primários
- Estima uma “média” ou um “efeito comum”
- Parte opcional de uma revisão sistemática

# Metanálise

## Porque fazer?

- Quantifica efeitos de tratamento e sua incerteza
- Aumenta o poder estatístico
- Aumenta a precisão
- Explora diferenças entre estudos
- Resolve controvérsias entre estudos com resultados conflitantes
- Gera novas hipóteses



# Metanálise

Quando é possível fazer?

- Mais de um estudo mediu um determinado efeito
- Os estudos são suficientemente similares para produzir um resultado significativo e útil
- O efeito (resultado) foi medido de forma similar
- Os dados estão disponíveis de forma que se possa usá-los



# Estudos experimentais      ENSAIO CLÍNICO

- OBJ: Avaliar terapias ou outras intervenções – padrão ouro
- Fornece evidência de **causa – efeito**
- Presença de dois ou mais grupos, que diferem em relação a uma **intervenção**, controlada pelo pesquisador:

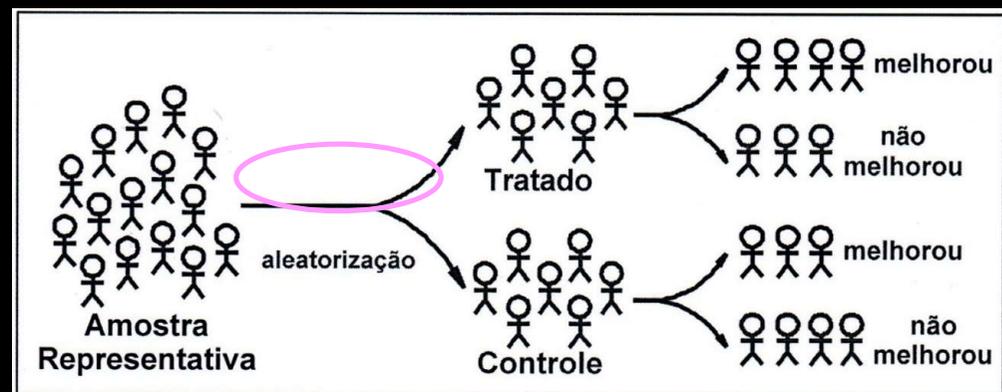
Exposição a um fator de risco

Dieta específica

Orientação

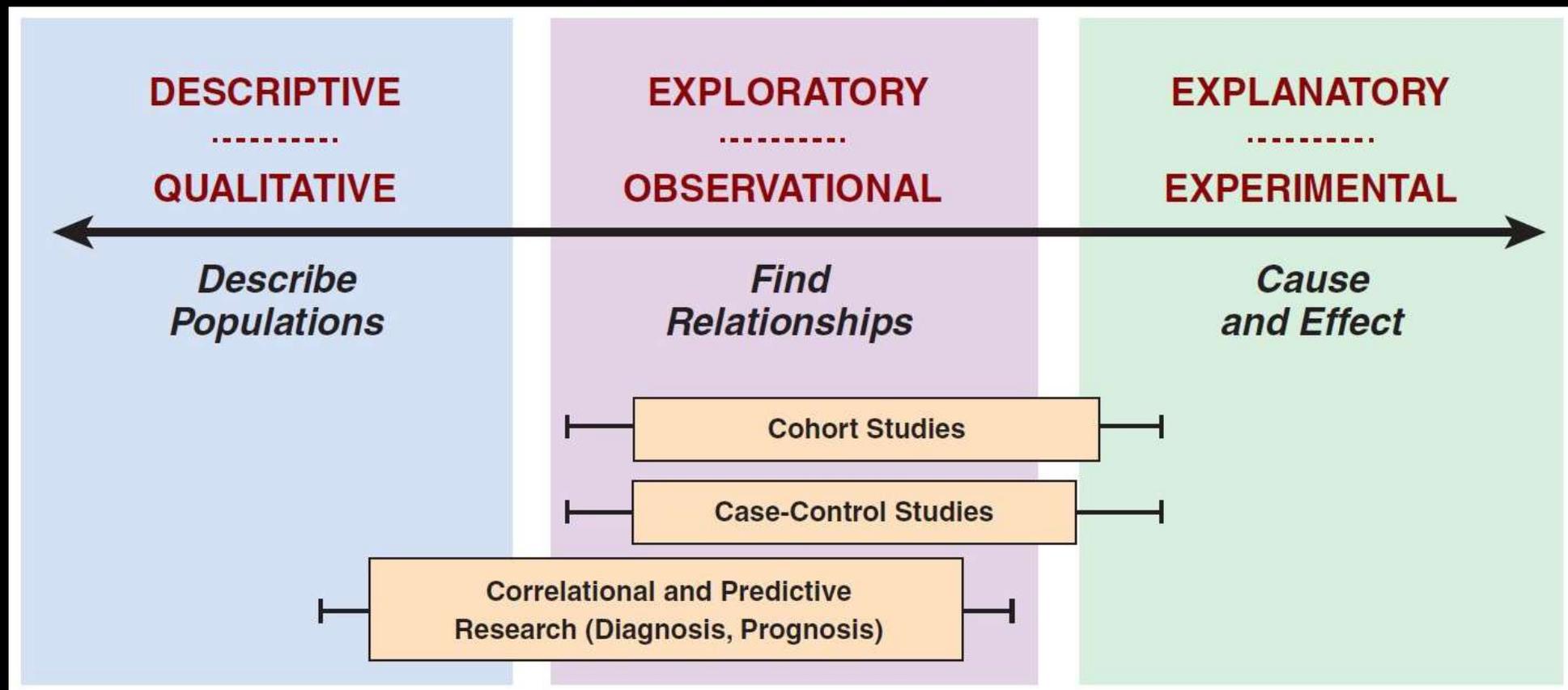
Tratamento medicamentoso

Cirurgia



- Grupos são acompanhados para observação do desfecho

# Desenhos de estudo



# Principais desenhos de estudo em pesquisas biomédicas

DESENHO		FINALIDADE	
Experimental	Animais	Experimento em animais	Comparar terapêuticas
	Humanos	Ensaio clínico	
Observacional	Analítico	Coorte	Identificar etiologia, fatores de risco e prognóstico
		Caso-controle	
		Revisão sistemática Metanálise	Combinar resultados de estudos já realizados
	Não analítico (Descritivo)	Transversal	Medir prevalência Gerar hipóteses
		Série de casos	Doenças raras
		Relato de caso	Doenças novas

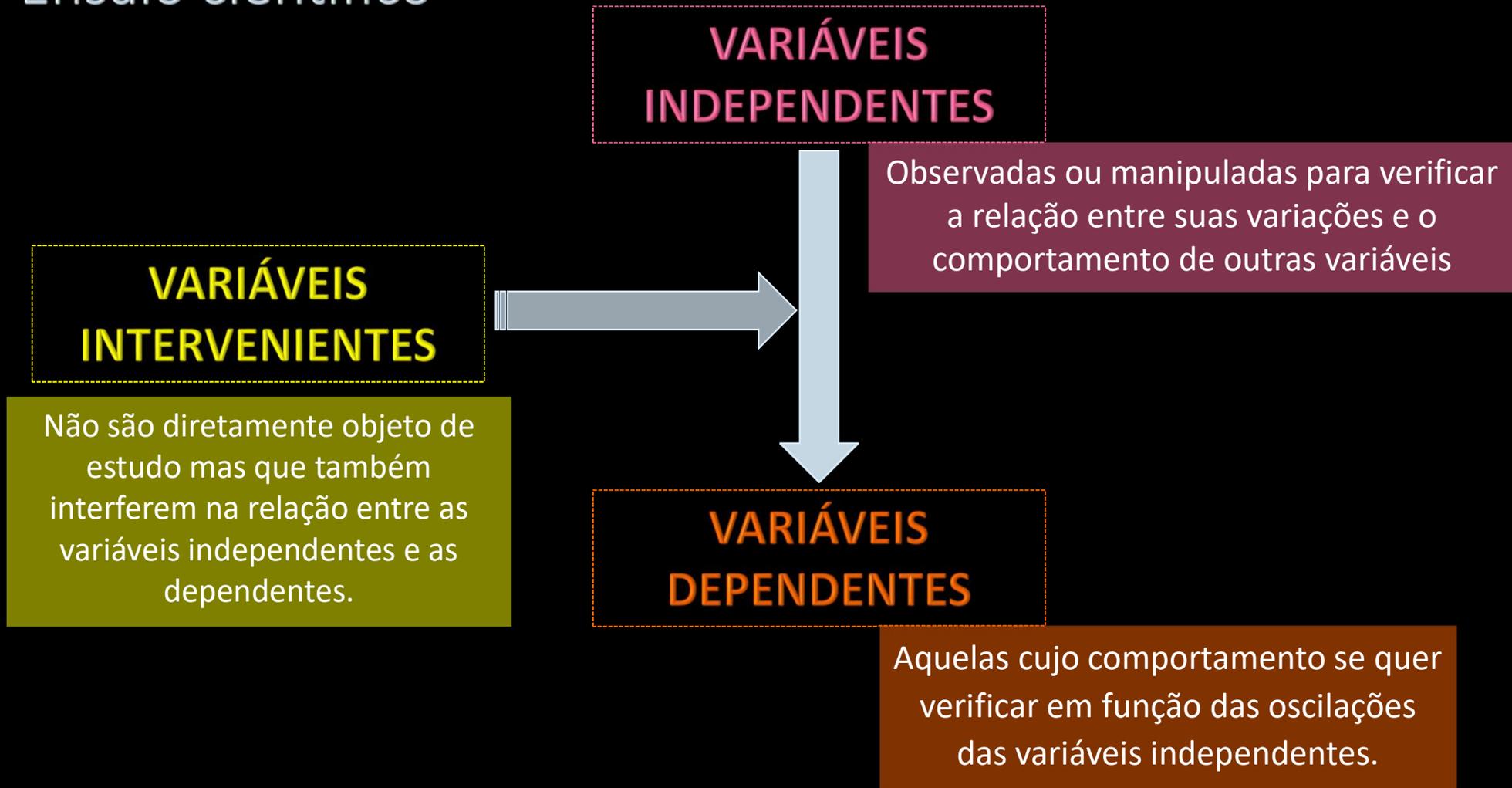
# PESQUISA



# Ensaio científico

Sequência de procedimentos na qual o pesquisador observa /  
manipula **VARIÁVEIS INDEPENDENTES** e verifica o  
comportamento das **VARIÁVEIS DEPENDENTES**, controlando o  
efeito de **VARIÁVEIS INTERVENIENTES**.

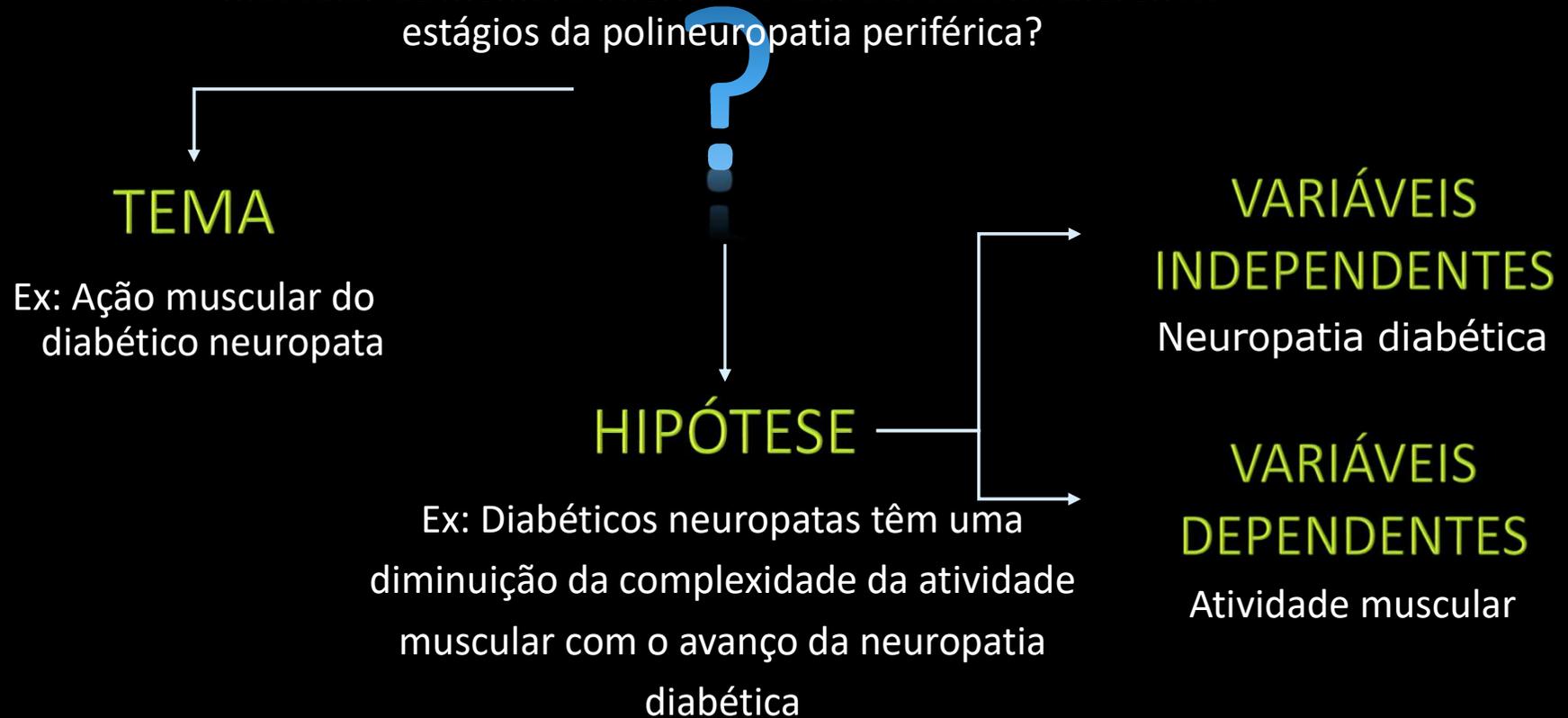
# Ensaio científico



# Etapas do projeto de pesquisa

- DEFINIÇÃO DA TEMÁTICA
- DEFINIÇÃO DO PROBLEMA
- DEFINIÇÃO DAS HIPÓTESES

Ex: Como é a complexidade dos padrões de recrutamento muscular de membro inferior de diabéticos com diferentes estágios da polineuropatia periférica?



## OBJETIVO

Avaliar a **complexidade** da EMG de ALTA DENSIDADE durante a contrações isométricas de baixa intensidade em indivíduos diabéticos com diferentes graus de neuropatia periférica (PND)

Complexidade  
do EMG

Magnitude da variabilidade

RMS do EMG

Estrutura da variabilidade

*Sample entropy* do EMG

## HIPÓTESES

- (i) PND umenta a magnitude da variabilidade do EMG,
- (ii) PND reduz a estrutura da variabilidade do EMG,
- (iii) Alterações são agravadas com a progressão da doença