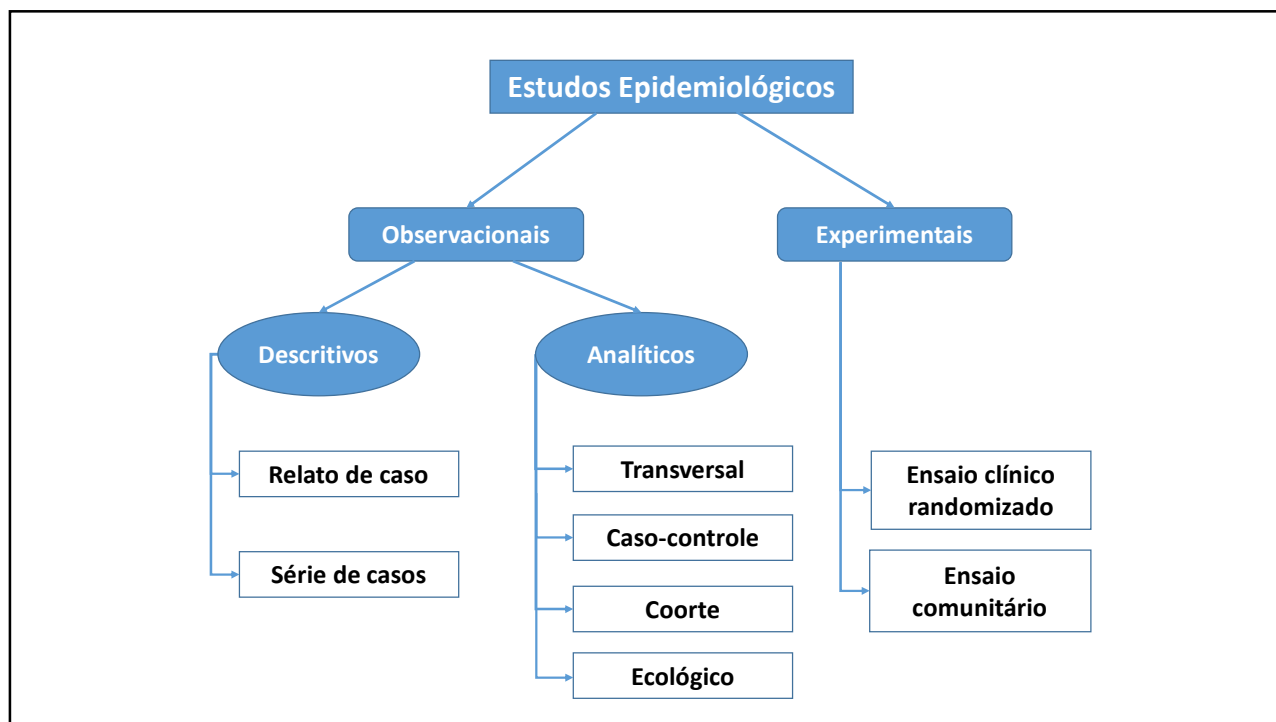




## Aplicação do método epidemiológico nos estudos das doenças infecciosas.

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Unidade Análise	Alocação de exposições	Desenho de Estudo Epidemiológico	Propósito
Grupos / comunidades	Observacional	Ecológicos	Descritivo / Analítico
	Experimental	Ensaio comunitários o de comunidades	Analítico
Indivíduos	Observacional	Reporte o Series de casos	Descritivos
		Corte transversal o estudo de prevalência	Descritivo / Analítico
		Estudo de Casos e Controles	Analítico
		Estudos de Coorte	Descritivo / Analítico
	Experimental	Ensaio clínicos	Analítico

Medida de Associação	Desenho de Estudo Epidemiológico		
	Ensaio Clínicos / Coortes	Corte Transversal	Casos e controles
Risco Relativo	✓		
Razão de taxas	✓		
Razão de Prevalências		✓	
Odds Ratio	✓	✓	✓

## Estudo transversal: Usos

- Descrever a frequência de doenças;
- Medir a frequência e características de fatores de risco conhecidos;
- Hipótese sobre novos fatores de risco;
- Planejar serviços e programas de saúde.
- Ponto de início para estudos prospectivos.

**medRxiv**  
THE PREPRINT SERVER FOR HEALTH SCIENCES



**BMJ** Yale

### **Integrating epidemiological and clinical predictors of SARS-CoV-2 infection in students and school staff in the state of São Paulo**

 Fredi A. Diaz Quijano,  José Mário Nunes da Silva, Tatiana Lang D'Agostini, Jéssica Pires de Camargo, Nathalia Cristina Soares Franceschi Landi de Moraes, Ricardo Haddad, Maria Cecília Gomes Pereira,  Dimas Tadeu Covas, Regiane A. Cardoso de Paula

doi: <https://doi.org/10.1101/2021.06.21.21259213>

**This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**

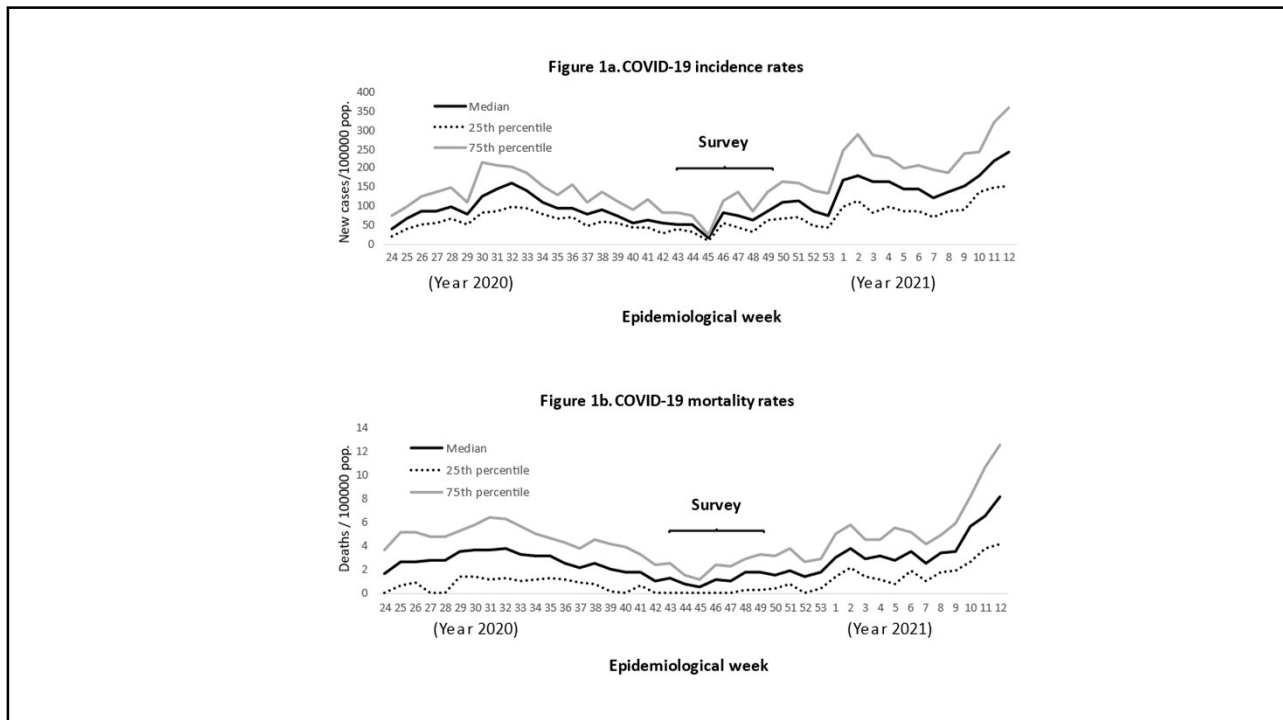
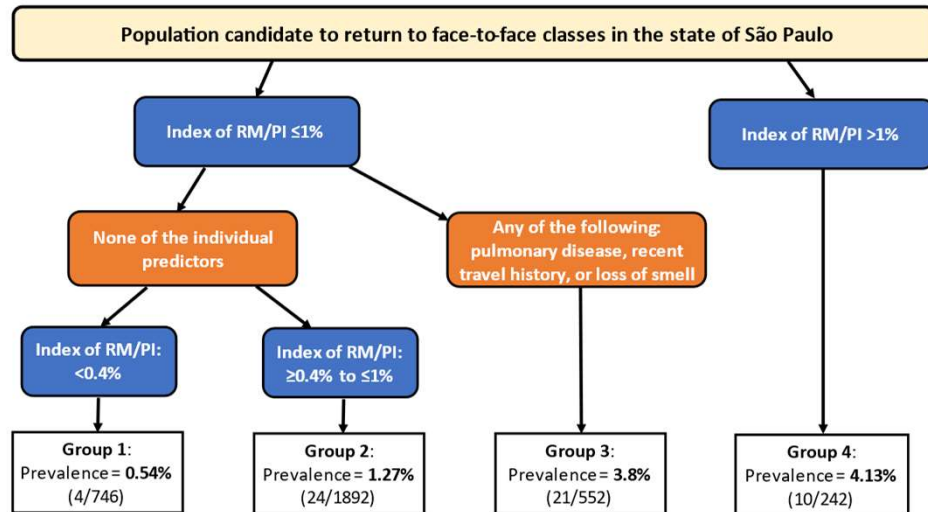
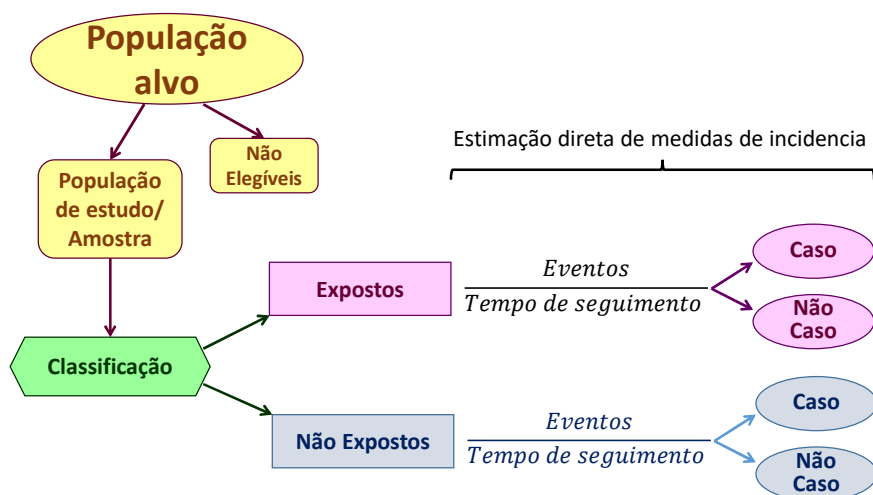


Table 3. Multiple model for predicting SARS-CoV-2 infection.		
Predictor	OR (95% CI)	p-value
RM/PI Index	1.45 (1.02 - 2.04)	0.04
Pulmonary disease	3.56 (1.56 - 8.11)	0.003
Loss of smell	5.12 (1.74 - 15.05)	0.003
Recent trip	2.13 (1.16 - 3.93)	0.02

Algorithm for classifying school population according to epidemiological and clinical variables associated with SARS-CoV-2 infection prevalence.

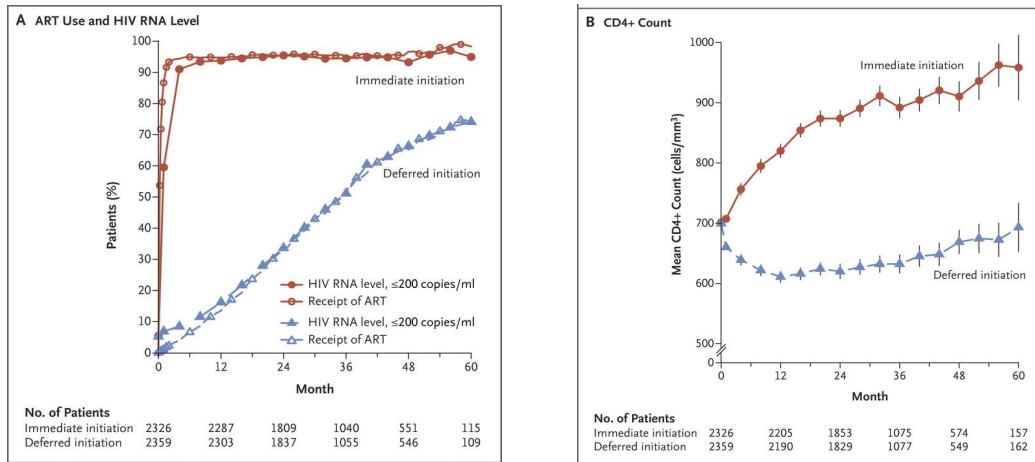


## Estudo de coorte



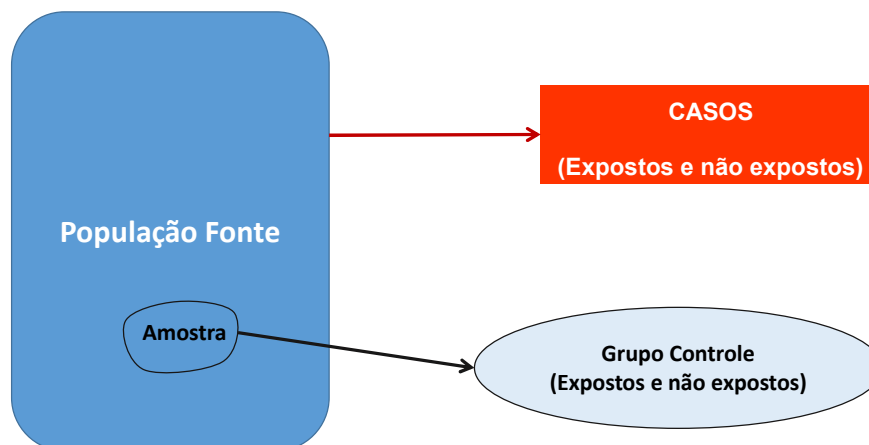
## Antiretroviral Therapy, HIV RNA Suppression, and CD4+ Count.

Shown are the percentages of patients who were receiving antiretroviral therapy (ART) and the percentages of patients who had an HIV RNA level of less than 200 copies per milliliter (Panel A) and the mean CD4+ count (Panel B) in the immediate-initiation group and the deferred-initiation group over a 5-year period.



The INSIGHT START Study Group. *N Engl J Med* 2015;373:795-807.

## Estudo de Caso Controle



*Retrospectivo ou Prospectivo*

**Table 3. Association of Oropharyngeal Cancer with Exposure to HPV and with Biomarkers of Cancer Associated with HPV-16.**

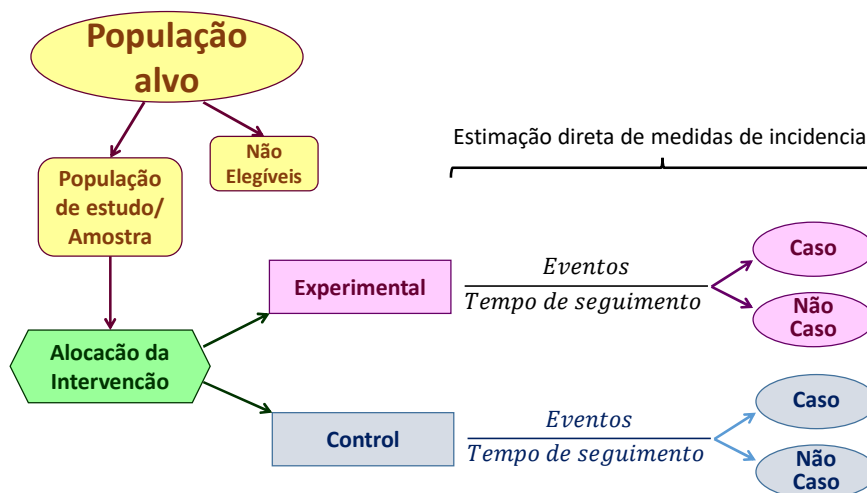
Measure of HPV Exposure or Disease	Prevalence		Odds Ratio (95% CI)	
	Case Patients (N=100) number (percent)	Control Patients (N=200) number (percent)	Unadjusted	Adjusted <sup>*</sup>
HPV-16 L1 serologic status				
Seronegative	43 (43)	186 (93)	1.00	1.00
Seropositive	57 (57)	14 (7)	17.6 (8.8–34.5)	32.2 (14.6–71.3)
Oral HPV-16 infection <sup>†</sup>				
Negative	68 (68)	192 (96)	1.00	1.00
Positive	32 (32)	8 (4)	11.3 (5.0–25.7)	14.6 (6.3–36.6)
Any oral HPV infection <sup>‡</sup>				
Negative	63 (63)	189 (94)	1.00	1.00
Positive	37 (37)	11 (6)	10.0 (4.8–20.7)	12.3 (5.4–26.4)
HPV-16 E6 or E7 serologic status				
Seronegative for E6 and E7	36 (36)	192 (96)	1.00	1.00
Seropositive for E6 or E7	64 (64)	8 (4)	33.3 (16.2–68.6)	58.4 (24.2–138.3)
HPV-16 DNA in tumor				
Absent	28 (28)	—	—	—
Present	72 (72)	—	—	—

<sup>\*</sup> Odds ratios were adjusted for age, sex, tobacco use, alcohol use, dentition and toothbrushing, and presence or absence of a family history of head and neck cancer.

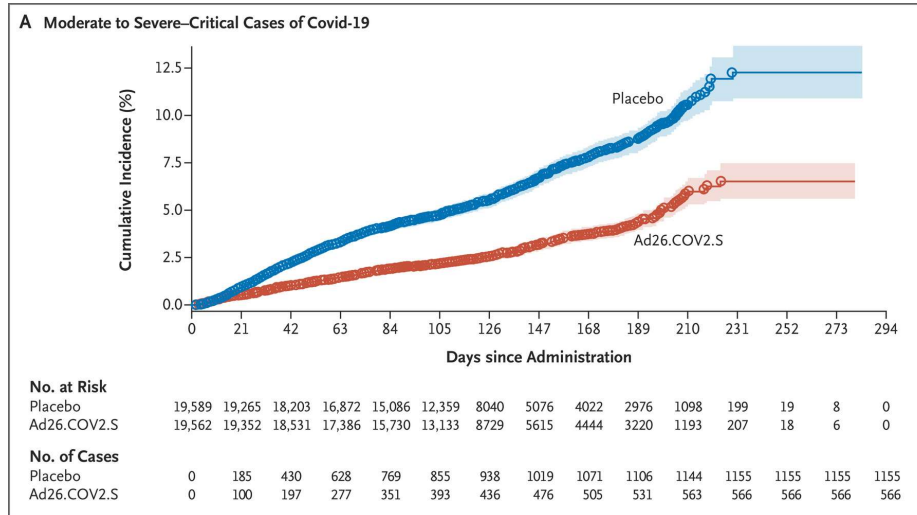
<sup>†</sup> Oral HPV-16 infection was detected with the use of a real-time PCR assay. The median number of cells analyzed for HPV DNA in case patients and control patients was similar (16,282 vs. 11,053 cells per 10- $\mu$ l sample;  $P=0.11$ ). The median HPV-16 viral load was 13.0 and 3.5 copies per 1000 cells among case patients and control patients who were positive for HPV-16, respectively.

<sup>‡</sup> Infection of the oral cavity with any of 37 types of HPV was detected with the use of consensus-primer PCR. The HPV types detected, in order of prevalence, were 16 (23 patients), 72 (4 patients), 62 (3 patients), 58 (2 patients), 6 (2 patients), and 18, 31, 51, 55, 61, 66, 68, and 73 (1 patient each) among case patients and 58 (2 patients), 62 (2 patients), and 6, 42, 51, 56, 61, 66, 68, 73, and CP6108 (1 patient each) among control patients. Seven case patients and two control patients were infected with multiple types of HPV.

## Ensaio Clínico



Sadoff J, et al. **Final Analysis of Efficacy and Safety of Single-Dose Ad26.COV2.S.**  
N Engl J Med. 2022 Mar 3;386(9):847-860. doi: 10.1056/NEJMoa2117608.



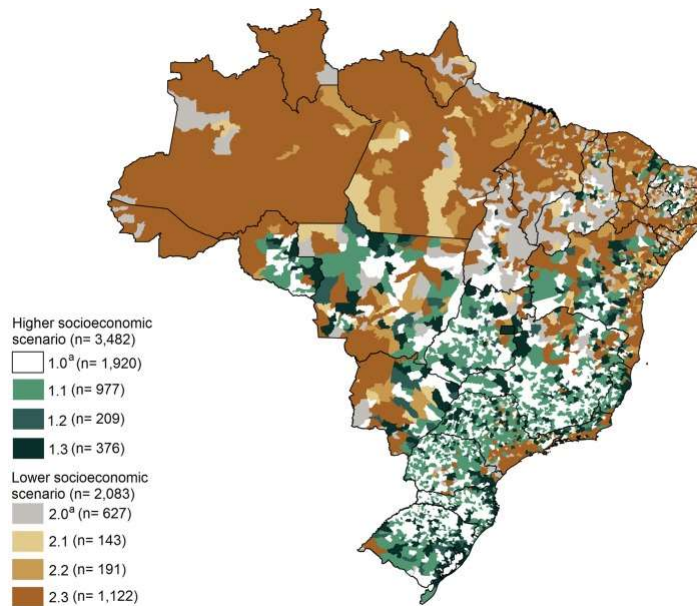
A single dose of Ad26.COV2.S provided 52.9% protection against moderate to severe–critical Covid-19.

## Estudos ecológicos

Tipos de variáveis:

1. **Medidas agregadas:** sintetizam características individuais dentro de cada grupo  
proporção de fumantes, taxa de incidência de uma doença, renda familiar média, Taxas de mortalidade
2. **Medidas ambientais:**  
características físicas do ambiente, nível de poluição do ar, qualidade da água, nível de radiação solar
3. **Medidas globais:** atributos de grupos, organizações ou lugares sem análogo no nível individual  
densidade demográfica, nível de desigualdade social, existência de determinado tipo de sistema de saúde



**Brazilian's municipalities by tuberculosis incidence rate scenario (2015).**

Pelissari DM, et.al. BMJ Open 2018; 8(6): e018545.

## ENSAIOS COMUNITÁRIOS

Avaliam intervenções em comunidades

A alocação, registro e aplicação da intervenção não são realizados individualmente, mas em comunidades específicas ou grupos de pessoas

...por exemplo, famílias, hospitais, centros de saúde, escolas, entre outros.

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JANUARY 23, 2014

VOL. 370 NO. 4

## A Trial of Mass Isoniazid Preventive Therapy for Tuberculosis Control

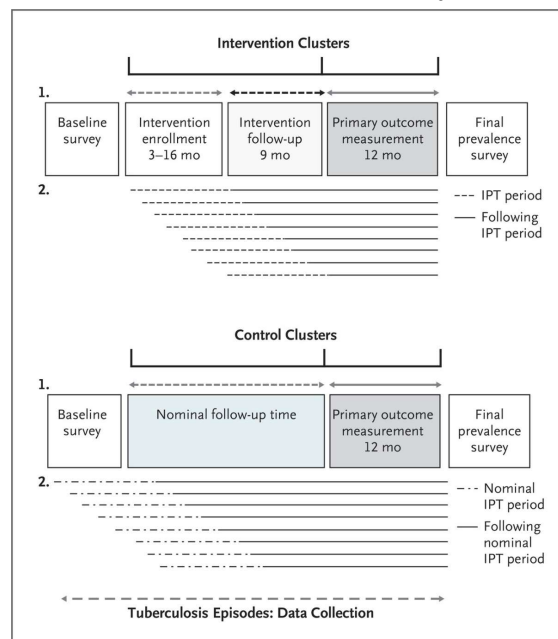
Gavin J. Churchyard, M.B., B.Ch., Ph.D., Katherine L. Fielding, Ph.D., James J. Lewis, Ph.D., Leonie Coetzee, D.Soc.Sc., Elizabeth L. Corbett, M.B., B.Chir., Ph.D., Peter Godfrey-Faussett, F.R.C.P., Richard J. Hayes, D.Sc., Richard E. Chaisson, M.D., and Alison D. Grant, M.B., B.S., Ph.D., for the Thibela TB Study Team

15 clusters with 78,744 miners as either intervention (40,981 miners in 8 clusters) or control clusters (37,763 miners in 7 clusters).

Intervention: all miners were offered tuberculosis screening. If active tuberculosis was diagnosed, they were referred for treatment; if not, they were offered 9 months of isoniazid preventive therapy.

The primary outcome was the cluster-level incidence of tuberculosis during the 12 months after the intervention ended.

## A Trial of Mass Isoniazid Preventive Therapy for Tuberculosis Control



## A Trial of Mass Isoniazid Preventive Therapy for Tuberculosis Control

**Table 2. Overall Effect of Community-wide Isoniazid Preventive Therapy: Tuberculosis Incidence and Prevalence.**

Outcome	Control Clusters		Intervention Clusters		Rate Ratio (95% CI) <sup>a</sup>			
	Cases <i>no./no. of person-yr</i>	Rate <i>per 100 person-yr</i> <sup>‡</sup>	Cases <i>no./no. of person-yr</i>	Rate <i>per 100 person-yr</i> <sup>‡</sup>	Unadjusted	P Value	Adjusted <sup>†</sup>	P Value
Primary outcome: tuberculosis incidence <sup>§</sup>								
Any	856/29,014	2.95	887/29,352	3.02	1.00 (0.75–1.34)	0.98	0.96 (0.76–1.21)	0.71

Churchyard GJ et al. N Engl J Med 2014;370:301-310.

Unidade Análise	Alocação de exposições	Desenho de Estudo Epidemiológico	Propósito
Indivíduos	Observacional	Reporte o Series de casos	Descritivos
		Corte transversal ou estudo de prevalência	Descritivo / Analítico
		Estudo de Casos e Controles	Analítico
		Estudos de Coorte	Descritivo / Analítico
	Experimental	Ensaio clínico	Analítico
Grupos / comunidades	Observacional	Ecológicos	Descritivo / Analítico
	Experimental	Ensaio comunitários o de comunidades	Analítico

## Alguns desafios metodológicos do estudo das doenças infecciosas

1. Definir o papel da infecção na questão de pesquisa
2. Como identificar e documentar as infecções
3. Qual parcela dos casos está sendo identificada ou selecionada.
4. Cobertura, completitude e qualidade das fontes de informação
5. Considerações para a análise e interpretação de resultados.

### Papel da infecção na questão de pesquisa

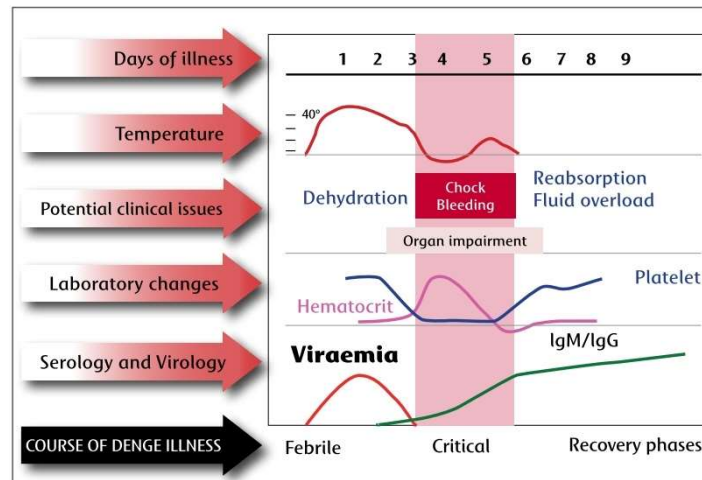
População { Exposição → Desfecho

- Em casos de tuberculose, efeito do tratamento sobre a mortalidade.
- Em adultos, associação entre infecção VPH e risco de câncer de orofaringe.
- Em população geral, efeito da vacinação sobre a incidência de sarampo.
- Em pessoas com VIH, o fluconazol redução do risco de candidíase.

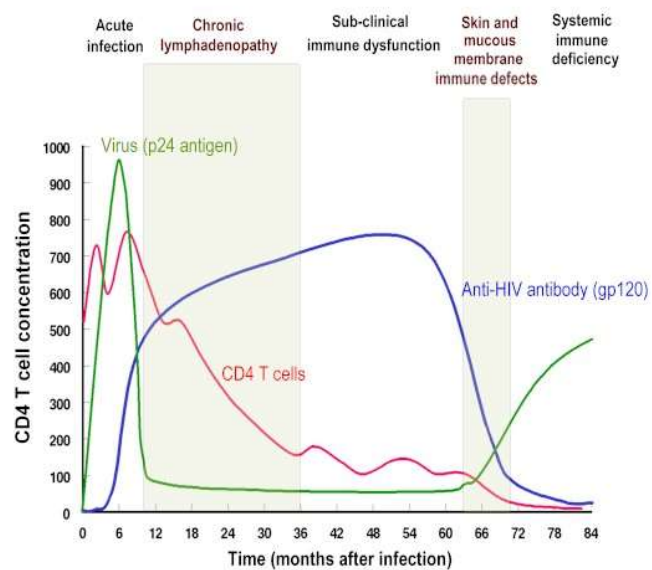
## Identificação da infecção segundo sua história natural

### 1.2. Course of the disease

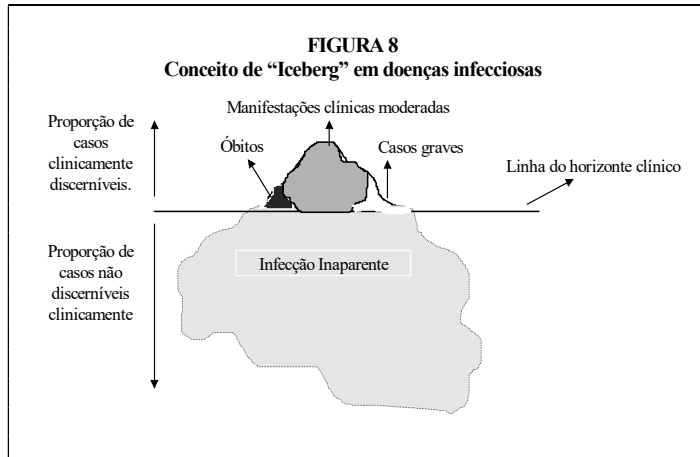
Figure 1. The course of dengue illness



## Identificação da infecção segundo sua história natural

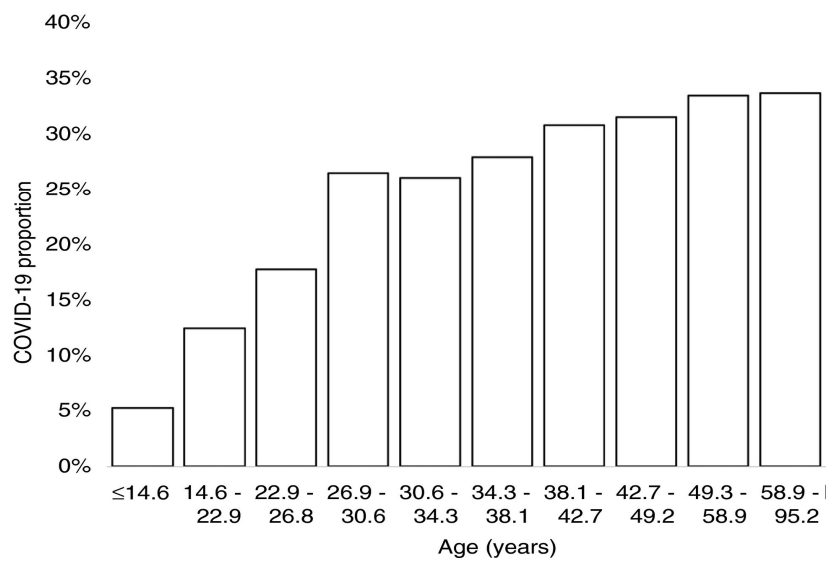


Qual parcela dos casos está sendo identificada e selecionada.



Dificuldade para diferenciar entre fatores associados com:

- **transmissão,**
- **manifestação,**
- **gravidade e**
- **detecção.**



Diaz-Quijano FA, et al. A model to predict SARS-CoV-2 infection based on the first three-month surveillance data in Brazil. [Tropical Med Int Health](#), Volume: 25, Issue: 11, Pages: 1385-1394, First published: 13 August 2020, DOI: (10.1111/tmi.13476)

## Cobertura, completitude e qualidade das fontes de informação

- Estudos prospectivos são ideais para identificação de casos incidentes. Mas são caros.
- Os estudos transversais (ex. soroepidemiológicos) são uteis para estimar a extensão do agravo. Mas é difícil estabelecer relação temporal.
- Casos e controles são de utilidade para eventos raros mas tem grandes desafios na seleção de participantes e mensuração das variáveis.
- Dados de vigilância podem permitir levantar coortes retrospectivas e outros desenhos com dados individuais, e fazer estudos ecológicos. No entanto, a qualidade da informação está sujeita aos determinantes da detecção de casos, notificação e preenchimento.

“Surveillance is the ongoing, systematic collection, analysis, and interpretation of health data used in the planning, implementation, and evaluation of public health programs”

(WHO, 1996)

- Os dados são usados para monitorar tendências para
  - Identificar epidemias
  - Alertar aos profissionais da saúde sobre as mudanças
  
- Estimar a magnitude da morbidade e mortalidade
  
- Apoiar a pesquisa epidemiológica.
  - Investigação de determinantes da situação de saúde
  - Avaliação do impacto das intervenções implementadas



Tomada de decisões

www2.datasus.gov.br/DATASUS/index.php?area=0203&id=29878153

Opções selecionadas:  
Doenças e Agravos de Notificação - De 2007 em diante (SINAN)

- Acidente por Animais Peçonhentos
- Botulismo
- Cólera
- Coqueluche
- Dengue até 2013
- Dengue de 2014 em diante
- Difteria
- Doença de Chagas Aguda
- Doenças Exantemáticas
- Esquistossomose
- Febre Amarela
- Febre Maculosa
- Febre Tifoide
- Hantavirose
- Hepatite
- Influenza Pandêmica
- Intoxicação Exógena
- Leishmaniose Visceral
- Leishmaniose Tegumentar Americana
- Leptospirose
- Malária
- Meningite
- Peste
- Paralisia Flácida Aguda
- Raiva
- Sífilis em Gestante
- Sífilis Congênita
- Síndrome da Rubéola Congênita
- Tétano Acidental
- Tétano Neonatal
- Violência doméstica, sexual e/ou outras violências

Indicadores de Saúde e Pactuações

Assistência à Saúde

▶ Epidemiológicas e Morbidade

Rede Assistencial

Estatísticas Vitais

Demográficas e Socioeconômicas

Inquéritos e Pesquisas

Saúde Suplementar

Estatísticas de acesso ao TABNET

Tutorial

Módulo gráfico/mapa do TABNET

Informações Financeiras

Serviços



# Global, regional, and national burden of tuberculosis, 1990–2016: results from the Global Burden of Diseases, Injuries, and Risk Factors 2016 Study

GBD Tuberculosis Collaborators\*



## Summary

**Background** Although a preventable and treatable disease, tuberculosis causes more than a million deaths each year. As countries work towards achieving the Sustainable Development Goal (SDG) target to end the tuberculosis epidemic by 2030, robust assessments of the levels and trends of the burden of tuberculosis are crucial to inform policy and programme decision making. We assessed the levels and trends in the fatal and non-fatal burden of tuberculosis by drug resistance and HIV status for 195 countries and territories from 1990 to 2016.

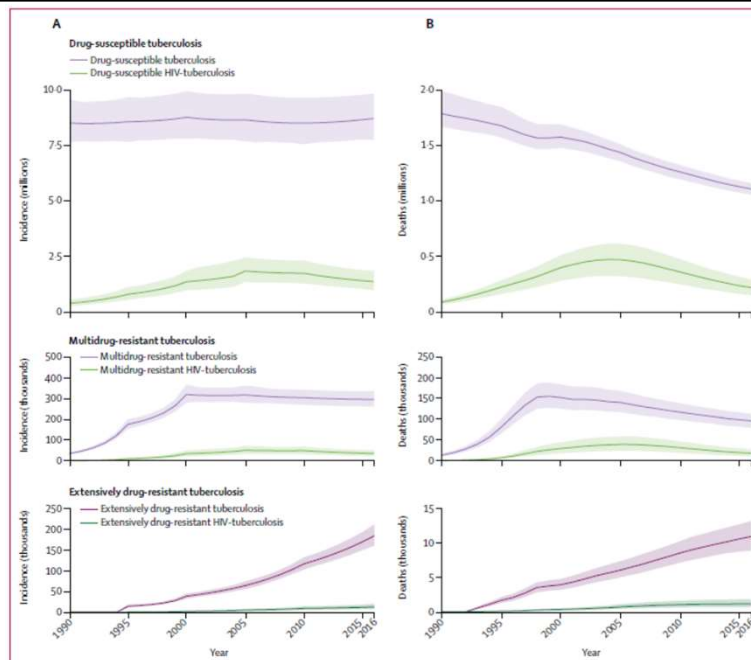
**Methods** We analysed 15 943 site-years of vital registration data, 1710 site-years of verbal autopsy data, 764 site-years of sample-based vital registration data, and 361 site-years of mortality surveillance data to estimate mortality due to tuberculosis using the Cause of Death Ensemble model. We analysed all available data sources, including annual case notifications, prevalence surveys, population-based tuberculin surveys, and estimated tuberculosis cause-specific mortality to generate internally consistent estimates of incidence, prevalence, and mortality using DisMod-MR 2.1, a Bayesian meta-regression tool. We assessed how the burden of tuberculosis differed from the burden predicted by the Socio-demographic Index (SDI), a composite indicator of income per capita, average years of schooling, and total fertility rate.

*Lancet Infect Dis* 2018;  
18: 1329–49

See [Comment](#) page 1291

\*Collaborators listed at the end of the Article

Correspondence to:  
Prof Christopher J L Murray,  
Institute for Health Metrics  
and Evaluation, Seattle,  
WA 98121, USA  
[cjlm@uw.edu](mailto:cjlm@uw.edu)



**Figure 1: Global tuberculosis incidence (A) and mortality (B) by drug-resistance type and HIV status, 1990–2016**  
Dark lines are estimates and shaded areas are 95% uncertainty intervals. HIV-tuberculosis=tuberculosis in individuals with HIV/AIDS. Multidrug-resistant tuberculosis=multidrug-resistant tuberculosis without extensive drug resistance.

*Am J Trop Med Hyg*, 86(2), 2012, pp. 328-334  
doi:10.4269/ajtmh.2012.11-0074  
Copyright © 2012 by The American Society of Tropical Medicine and Hygiene

## Factors Associated with Dengue Mortality in Latin America and the Caribbean, 1995–2009: An Ecological Study

Fredi Alexander Díaz-Quijano\* and Eliseu Alves Waldman

*Faculdade de Saúde Pública, University of São Paulo School of Public Health, São Paulo, Brazil;*  
*Grupo Latinoamericano de Investigaciones Epidemiológicas,*  
*Organización Latinoamericana para el Fomento de la Investigación en Salud (OLFIS), Bucaramanga, Colombia*

**Abstract.** In this study, we aimed to estimate the effect that environmental, demographic, and socioeconomic factors have on dengue mortality in Latin America and the Caribbean. To that end, we conducted an observational ecological study, analyzing data collected between 1995 and 2009. Dengue mortality rates were highest in the Caribbean (Spanish-speaking and non-Spanish-speaking). Multivariate analysis through Poisson regression revealed that the following factors were independently associated with dengue mortality: time since identification of endemicity (adjusted rate ratio [aRR] = 3.2 [for each 10 years]); annual rainfall (aRR = 1.5 [for each  $10^3$  L/m<sup>2</sup>]); population density (aRR = 2.1 and 3.2 for 20–120 inhabitants/km<sup>2</sup> and > 120 inhabitants/km<sup>2</sup>, respectively); Human Development Index > 0.83 (aRR = 0.4); and circulation of the dengue 2 serotype (aRR = 1.7). These results highlight the important role that environmental, demographic, socioeconomic, and biological factors have played in increasing the severity of dengue in recent decades.

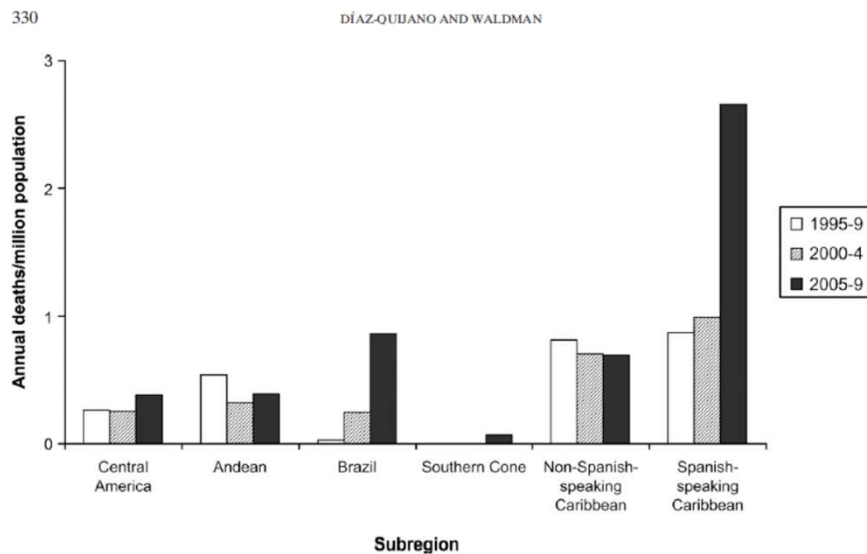


FIGURE 1. Dengue-related mortality, which included suspected and laboratory-confirmed cases, in Latin America and the Caribbean, by subregion, 1995–2009.

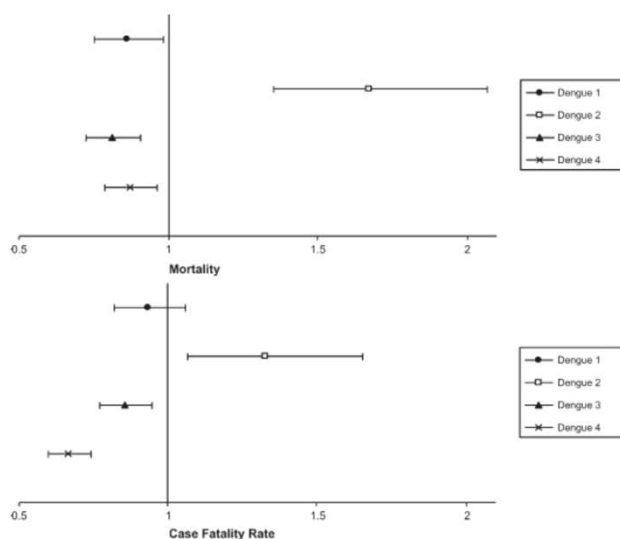


FIGURE 3. Rate ratios (with 95% confidence interval) for dengue mortality and dengue case fatality rate, associated with circulating serotypes. Estimates were adjusted for subregion, age of endemicity, rainfall, population density, and Human Development Index.

## RESEARCH AND PRACTICE

# Zika-Associated Microcephaly Epidemic and Birth Rate Reduction in Brazilian Cities

Fredi Alexander Diaz-Quijano, MD, PhD, Daniele Maria Pelissari, MSc, and Alexandre Dias Porto Chiavegatto Filho, PhD

**Objectives.** To estimate birth reduction potentially in response to Zika virus–associated microcephaly among the 36 largest Brazilian cities.

**Methods.** We analyzed the number of live births per month on the basis of information on approximately 8.2 million births from all of Brazil’s state capitals and cities that had more than 10 000 annual births.

**Results.** In the second half of 2016, the live birth rate was reduced by 7.78% (95% confidence interval [CI] = 6.64%, 8.89%;  $P < .001$ ). This reduction was correlated with the Zika virus–associated microcephaly rate. In the cities with the highest microcephaly rate in 2015 (> 1 case per 1000 live births), the reduction in the live birth rate was 10.84% (95% CI = 8.58%, 13.04%).

the Information System on Live Births (Sistema de Informação sobre Nascidos Vivos) of the Brazilian Ministry of Health (last updated May 3, 2017). We obtained data on ZIKV-associated microcephaly from the Brazilian National Information System for Notifiable Diseases (Sistema de Informação de Agravos de Notificação).

Using a negative binomial regression model and birth data from January 2007 to June 2016, we estimated the expected number

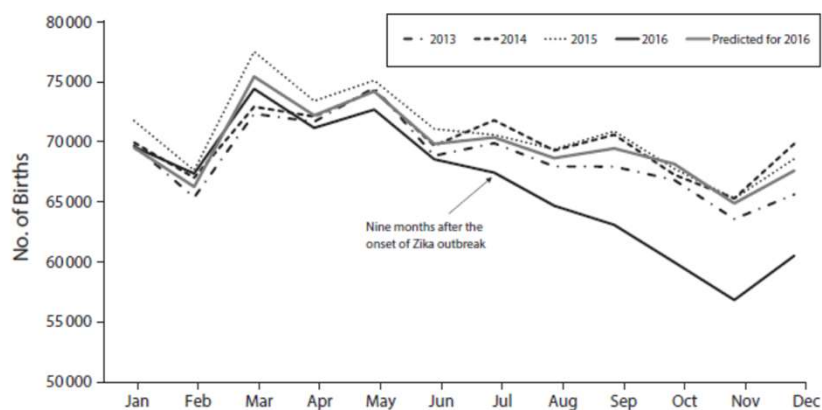


FIGURE 1—Sum of Predicted and Observed Births by Year and Month: 36 Brazilian Cities, 2013–2016

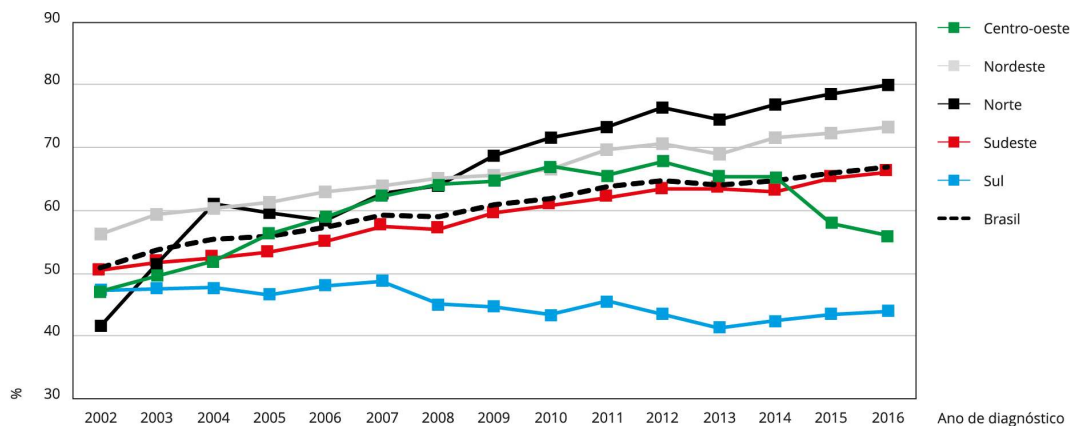
### Cadastro Nacional de Estabelecimentos de Saúde como ferramenta de análise da descentralização do atendimento da tuberculose para a atenção básica

Brazilian National Registry of Healthcare Establishments as a tool for the analysis of decentralization of tuberculosis treatment to basic care services

Registro Nacional de Establecimientos de Salud como herramienta de análisis de la descentralización de la atención a la tuberculosis en la atención básica

*Daniele Maria Pelissari*<sup>1,2</sup>  
*Marina Gasino Jacobs*<sup>1</sup>  
*Parricia Bartholomay*<sup>1</sup>  
*Marli Souza Rocha*<sup>1</sup>  
*Draurio Barreira*<sup>3</sup>  
*Denise Arakaki-Sanchez*<sup>1</sup>  
*João Paulo Toledo*<sup>4</sup>  
*Fredi Alexander Diaz-Quijano*<sup>2</sup>

### Percentual de casos novos de tuberculose\* atendidos na Atenção Básica. Brasil e macrorregiões.



\* Elegíveis para serem acompanhados na atenção básica.

Pelissari DM, Jacobs MG, Bartholomay P, Rocha MS, Barreira D, Arakaki-Sanchez D, Toledo JP, Diaz-Quijano FA. Cad Saúde Pública 2018; 34(12):e00173917

## Atendimento adequado dos pacientes

### Exemplos:

A cultura de micobactéria é recomendada a todas as pessoas com suspeita de tuberculose (TB) submetidas à baciloscopia ou diagnosticadas pelo TRM-TB.

A testagem para HIV é recomendada a todos os casos de TB

No entanto, a adesão a essas recomendações é desigual.



## Original Research

## Macrodetermined racial inequalities in diagnostic testing among tuberculosis patients in Brazil



M.G. Jacobs<sup>a,\*</sup>, D.M. Pelissari<sup>a</sup>, F.A. Diaz-Quijano<sup>b</sup>

<sup>a</sup> National Tuberculosis Programme, Ministry of Health, PO 700 – SKTVN 702, Via W 5 Norte, 6º Andar, Brasília, DF, Brazil

<sup>b</sup> Department of Epidemiology, School of Public Health, University of São Paulo. Av. Dr. Arnaldo, 715 - Cerqueira César, São Paulo, SP, Brazil

## ARTICLE INFO

## Article history:

Received 27 February 2018

Received in revised form

25 October 2018

Accepted 5 November 2018

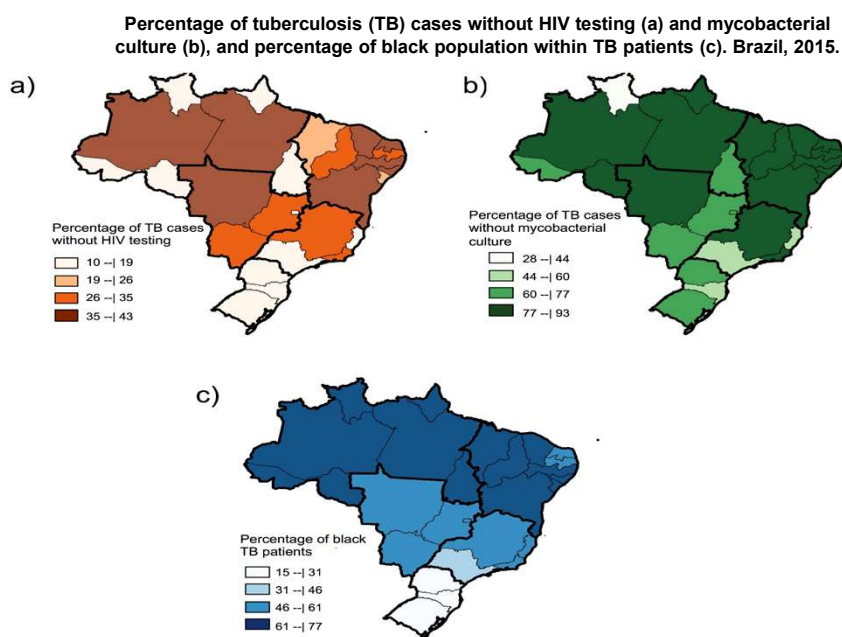
Available online 15 January 2019

## ABSTRACT

**Objectives:** To estimate the association between tuberculosis (TB) patients' race and patients' access to diagnostic testing in Brazil. In addition, we evaluated if the associations could be explained by a geographic codistribution between racial groups and diagnostic testing.

**Study design:** It is a cross-sectional study based on secondary data from a national surveillance system of new TB cases diagnosed in 2015.

**Methods:** We evaluated the association between TB patients' race (independent variable)



### **Pesquisa aninhada na vigilância: Algumas vantagens**

- ✓ Aproveita recursos
- ✓ Abrangência
- ✓ Oportuna (Timeliness)
- ✓ Foco em doenças priorizadas
- ✓ Apoio institucional

### **Limitações e desafios dos dados de vigilância**

Subnotificação multideterminada

Completitude e qualidade dos dados

Dificuldade para ligar dados individuais de diferentes fontes

Omissão de variáveis que podem ser essenciais

## **Considerações para a análise e interpretação de resultados.**

- A correlação entre eventos (infecções) faz com que tendam a não ser independentes.
- Impossibilidade para avaliar efeitos de determinantes em grupos sem os elementos mínimos para a infecção acontecer.
- O risco de vieses relacionados aos algoritmos diagnóstico.
- Os vieses de seleção dependentes da restrição ou condicionamento por manifestações da doença (collider bias).
- A variabilidade dos determinantes que dificulta fazer projeções, por ex, em modelagem matemática.

## **Conclusões**

Além dos inerentes de cada desenho de estudo epidemiológico, existem desafios específicos no estudo das doenças infecciosas.

Os sistemas de vigilância pode ser uma fonte principal ou complementar de dados para pesquisa em Saúde Pública.

Apesar das limitações, a pesquisa baseada em dados de vigilância pode fornecer insumos para tomada de decisões e levantar hipóteses serem abordadas por estudos subsequentes.