



# Diseño de Estudios de Investigación

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# Conflictos de Interés

▶ Ninguno

# Que podemos publicar?

- ▶ Cartas al editor
  - ▶ Comentarios a artículos científicos
  - ▶ Cartas científicas
- ▶ Estudios observacionales
  - ▶ El investigador no tiene control sobre las variables de estudio
- ▶ Estudios de Intervención
  - ▶ El investigador tiene control sobre la intervención a ser estudiada
- ▶ Estudios de diseño y evaluación de pruebas diagnósticas
  - ▶ Permiten la creación y/o validación de pruebas diagnósticas

# Cartas al editor

- ▶ Comentarios a artículos
- ▶ Cartas científicas (observaciones preliminares, estudios piloto)

■ Letter

# Letter to the Editor Regarding the Article: Relationship between Age at Menarche and Metabolic Syndrome in Premenopausal Women: Korea National Health and Nutrition Examination Survey 2013–2014

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## Dear Editor,

We read with great interest the article by Hwang et al.<sup>1)</sup> published in the September 2018 issue of the *Korean Journal of Family Medicine*.

The paper reported lack of an association between the age of menarche and metabolic syndrome in the Korean population as compared to other populations.<sup>2-4)</sup> However, we have some comments regarding the methodological issues.

First, we believe that by stratifying the multivariate analysis by age (20–39 and 40–55 years) as a categorical variable at the time of survey and then adjusting all models again using age as a numerical variable (see Table 3 in the study of Hwang et al.<sup>1)</sup>, the models would be overadjusted, which can affect the variations by falsely increasing the confidence intervals.<sup>5)</sup> This could explain why strong relationships with metabolic syndrome were not found in the multivariate analysis, contrary to the finding from the crude analysis, where women with menarche at younger than 12 years were found to have two times higher risk of developing a metabolic syndrome than women with ages of menarche between 12 and 15 years, as shown in Appendix 1 of Hwang et al.<sup>1)</sup> The later association is consistent

with findings of multiple previous studies.

Another remarkable finding is that although the risk of metabolic syndrome is almost twice as high in patients in the menarche group who were older than 16 years than in those in the menarche group who were younger than 12 years, the data in Table 2 of Hwang et al.<sup>1)</sup> show the frequency of individual values such as body mass index and abdominal circumference, which have a higher prevalence in women younger than 12 years. An explanation of this difference should have been provided in the Discussion section.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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CARTAS CIENTÍFICAS

Letter to the Editor

**Early conversion of tuberculin skin test in medical students who begin hospital practices**

Dear Editor,

Unperceived exposure to patients with tuberculosis (TB) is a common event in training staff in hospitals in high incidence countries, the risk of acquiring the disease at the hospital setting being 2–50 times higher than in the community.<sup>1</sup> Although medical students are a risk group for acquiring TB infection, most of all during the first months of contact with the hospital, neither universities nor teaching hospitals have guidelines or protocols to minimize it. To quantify this risk, we evaluate the early conversion of the tuberculin skin test (TST) as an indicator of primary TB infection in medical students after the beginning of their hospital practices.

The study population comprised medical students assigned to start their clinical practices in Reference Hospitals of Ministry of Health (MOH) or Social insurance (ESSALUD) in 2008. We obtained baseline data on gender, age, TB contact, body mass index (BMI) and use of N95 particulate respirators

For descriptive analysis, numeric variables are presented as medians and interquartile ranges, while categorical variables are presented as frequencies and percentages. Variables associated with TST conversion were assessed through Mann–Whitney, chi-square or Fisher exact test for numerical and categorical variables, respectively. The study was approved by the University Ricardo Palma and the ethics committee of Hospital Hipólito Unanue.

We included 60 students, 30 from the MOH hospital and 30 from the ESSALUD hospital. Out of them, 34 (57%; 95% CI 43–69%) were female; the median age was 21.5 years (IQR 20–24 years). None of the baseline characteristics differed between participants with positive ( $n = 23$ ) and negative ( $n = 37$ ) initial

TST result  
those stud  
(51.4%; 95%  
was 65% fe  
for studen

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# Reportes de Caso

- ▶ Enfermedades Raras (o no descritas previamente en el país).
- ▶ Presentación inusual de enfermedades comunes.



**AMP**

Acta Médica Peruana

**REPORTE DE CASOS**

# **Tromboembolismo pulmonar bilateral como presentación de un síndrome antifosfolipídico: un reporte de caso**

*Bilateral pulmonary thromboembolism as the presenting manifestation of the antiphospholipidic syndrome: report of a case*

Daniel Vásquez-Álvarez<sup>1,2,a</sup>, Johan Azañero-Haro<sup>3</sup>, Isabel Suni Jiménez-Casaverde<sup>2,4,a</sup>, Alonso Soto-Tarazona<sup>3,4,5</sup>

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a Médico Residente de Neumología.

## Histoplasmosis Gástrica simulando una úlcera gástrica maligna

Alonso Ricardo Soto Tarazona\*, José Luis Meza Flores\*\* , Doris Garrido Rivadeneyra\*\*\*,  
Jaime Cok Garcia\*\*\*\*

### RESUMEN

Se presenta el caso de un paciente joven que acude por dolor abdominal crónico, procedente de una zona endémica de Histoplasmosis, en quien se evidencia a la endoscopia digestiva alta la presencia de compromiso gástrico caracterizado por presencia de lesión úlcero infiltrante simulando un carcinoma. El diagnóstico final fue histoplasmosis diseminada crónica con compromiso gástrico . El paciente presentaba como condición subyacente hepatopatía alcohólica crónica . Se debe incluir a la histoplasmosis en el diagnóstico diferencial de lesiones ulceradas y/o infiltrantes del tracto gastrointestinal en pacientes provenientes de zonas endémicas o con condiciones de inmunosupresión predisponentes.

**PALABRAS CLAVE:** Histoplasmosis, Estómago, Úlcera.

# Estudios Observacionales

- ▶ Pueden ser descriptivos o analíticos

## **Descriptivos**

- ▶ Describen una o más características de una población dada

## **Analíticos**

- ▶ Evalúan la presencia de **asociación** entre dos o más variables

# Estudios Observacionales

- ▶ Reportes de casos/series de casos
- ▶ **Transversales**
- ▶ Casos y Controles
- ▶ Cohortes
- ▶ Ecológicos

# ESTUDIOS TRANSVERSALES

- ▶ Realizan la(s) medición(es) en un **punto de tiempo** determinado.
- ▶ Pueden ser descriptivos (de prevalencia) o **analíticos**.
- ▶ Útiles para evaluar prevalencia
- ▶ Medida de asociación : OR (o PR ).
- ▶ No pueden establecer temporalidad de la asociación entre dos factores.
- ▶ Se mide la EXPOSICIÓN y el posible EFECTO en un mismo momento

# Asociación entre depresión y disfunción sexual

	Depresión	No depresión
Disfunción sexual	70	30
No disfunción sexual	30	70

Razón de Prevalencia= Prevalencia en expuestos/Prevalencia en no expuestos  
 $\frac{70/100}{30/100} = 2.33$

Odds Ratio= Odds de disfunción sexual en deprimidos/Odds de disfunción sexual en no deprimidos  
 $\frac{70/30}{30/70} = 5.44$

# Estudios Observacionales

- ▶ Transversales
- ▶ **Casos y Controles**
- ▶ Cohortes
- ▶ Ecológicos

# Estudios de Casos y Controles

- ▶ Evalúan la presencia de una o más condiciones (exposiciones) **en pacientes con y sin enfermedad** (o efecto).
- ▶ La exposición debe tener un periodo de latencia razonable para producir el efecto.
- ▶ Elección de controles es muy importante para garantizar comparabilidad y evitar la presencia de factores confusores. Los controles deben ser representativos de la **población que dio origen a los casos**
- ▶ Especialmente útiles para la evaluación de factores asociados a enfermedades RARAS y/o con periodos de latencia muy prolongados.

# Es la circuncisión un factor protector para cáncer de pene?

	Cancer de Pene (n=100)	No cáncer de pene (n=400)
Circuncisión	20	160
Ausencia de circuncisión	80	240

Odds Ratio=  $\frac{\text{Odds de haber sido circuncidado en pacientes con cáncer de pene}}{\text{Odds de haber sido circuncidado en pacientes sin cáncer de pene}}$

$$\frac{20/80}{160/240} = 0.375$$

# Análisis de Estudios de Casos y Controles

## Medida de Asociación

Odds Ratio

## Interpretación

- ▶  $OR=1$
- ▶  $OR<1$  factor asociado a menor Odds (chance) del evento.
- ▶  $OR>1$  factor asociado a mayor Odds del Evento.

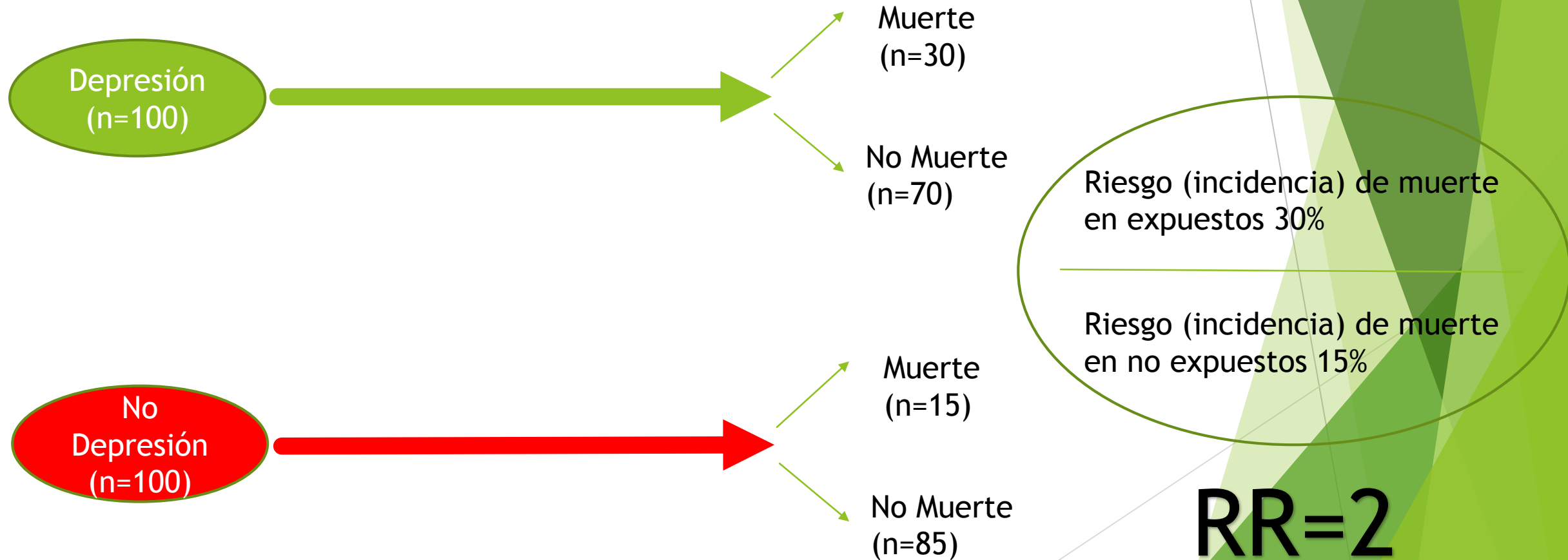
# Estudios de Cohortes

- ▶ En estos estudios se identifica **pacientes con y sin una exposición y se siguen en el tiempo** para evaluar el desarrollo de un efecto.
- ▶ Permiten establecer temporalidad.
- ▶ Permiten medir la **INCIDENCIA** del desarrollo de la condición.
- ▶ Medida de asociación : **Riesgo relativo (RR)**

Incidencia en expuestos

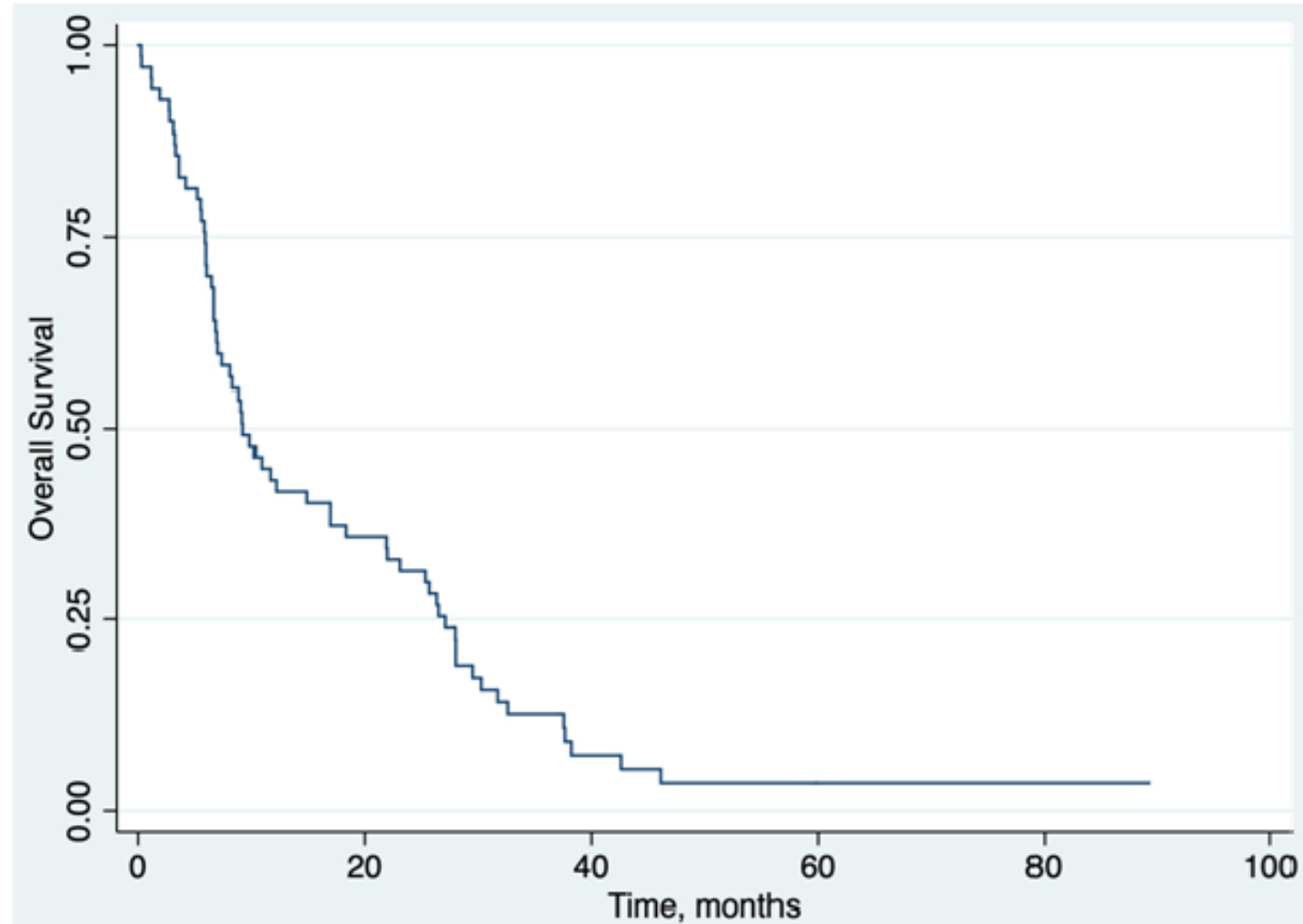
Incidencia en no expuestos

# Asociación entre síntomas depresivos y mortalidad tardía en pacientes hospitalizados



# Análisis de Sobrevida

- ▶ Tiempo hasta el desarrollo de un evento(muerte)
- ▶ Función de Sobrevida (supervivencia)
- ▶ Representación Gráfica: Curvas de Kaplan Meier
- ▶ Análisis Estadístico: Regresión de Cox
- ▶ Medida de Asociación:
- ▶ HAZARD RATIO (interpretación similar a RR)



## Original Article

# Survival and prognostic factors in non-small cell lung cancer patients with mutation of the EGFR gene treated with tyrosine kinase inhibitors in a peruvian hospital

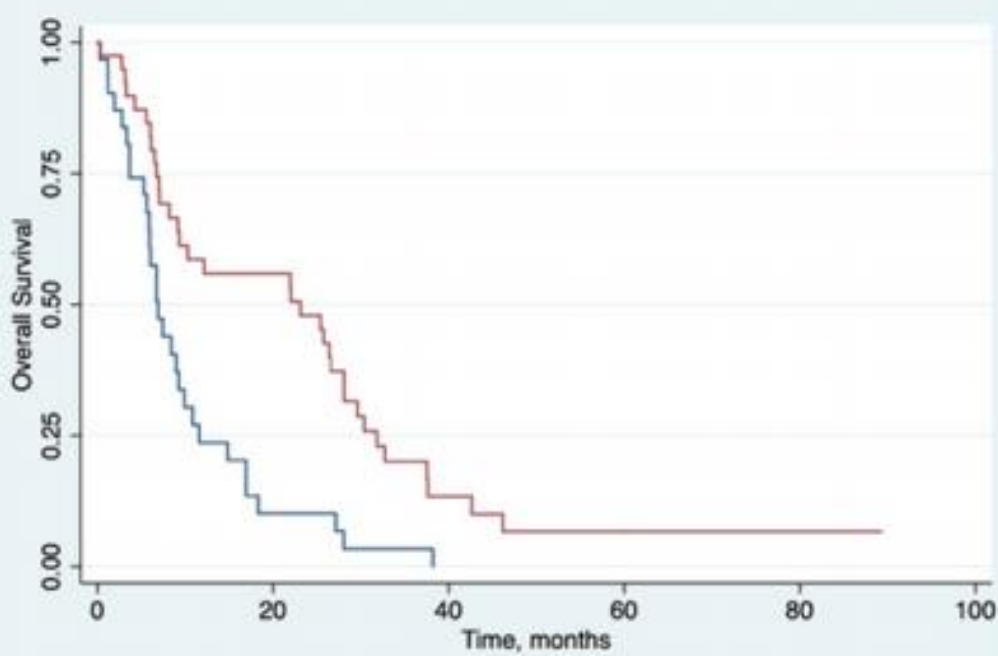
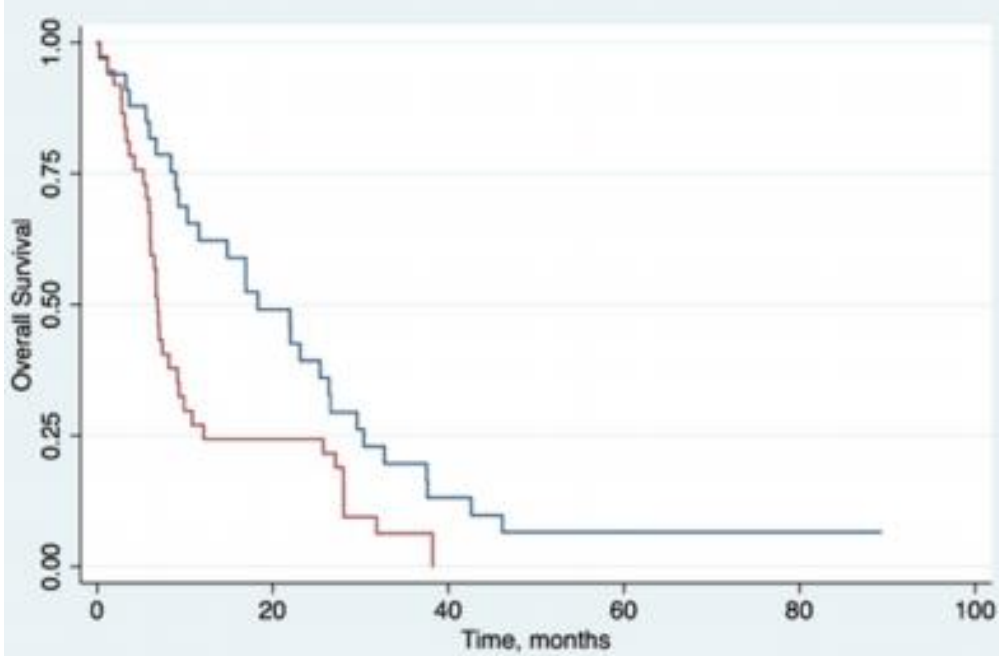
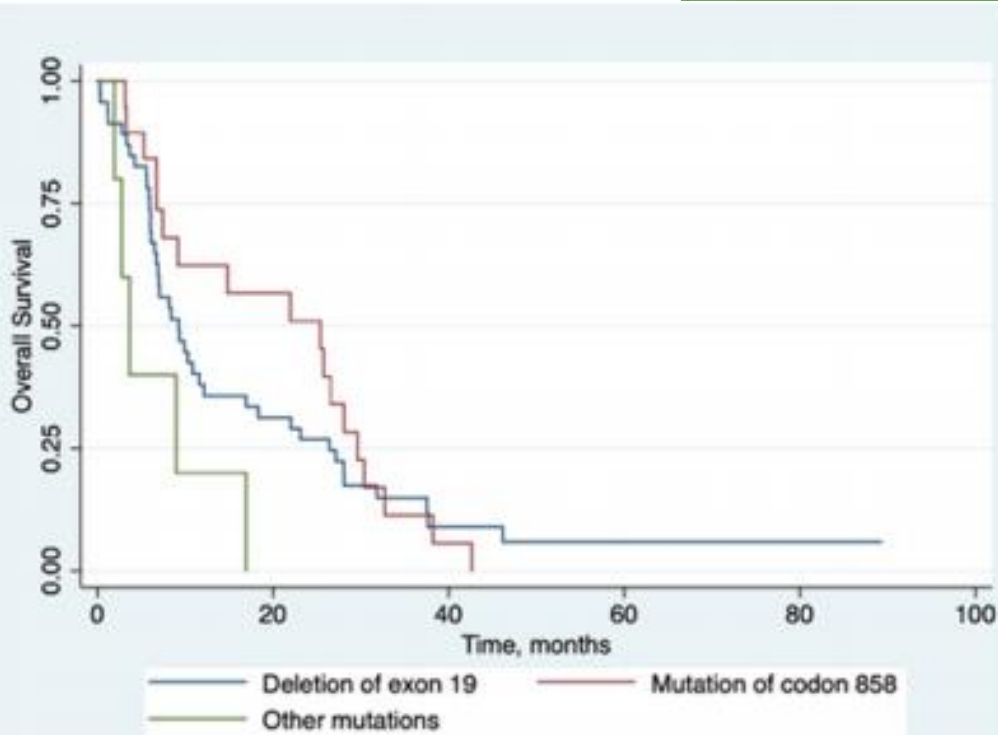
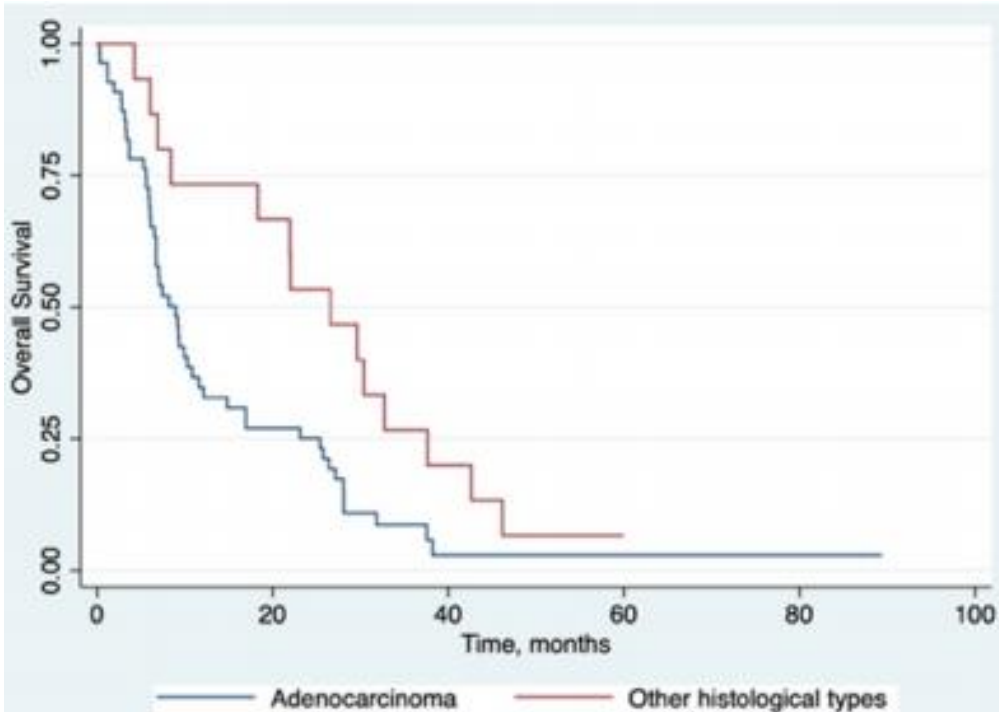
Ximena E Gómez<sup>1</sup>, Alonso Soto<sup>1,2</sup>, Marco A Gómez<sup>3</sup>

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**Abstract:** The identification of the epidermal growth factor mutation (EGFR) is a positive prognostic factor for survival and therapeutic response to tyrosine kinase inhibitors (TKIs) in patients with non-small cell lung cancer (NSCLC). TKIs are considered first line treatment in Patients with stages IIIB and IV NSCLC. We investigated the survival and prognostic factors in NSCLC patients with the mutation of the EGFR in routine clinical practice. We conducted a retrospective cohort observational study of 72 patients with non-small cell lung cancer (NSCLC) with EGFR gene mutations that received treatment with erlotinib from January 2009 to December 2015. Kaplan-Meier curves were presented. The association between independent variables and survival was analyzed using the Long-Rank test in bivariate analysis and for multivariate analysis, Cox proportional hazards method was used to calculate hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). We included data from 72 patients, which were followed for a total of 1144 patient-months. The majority of patients were female (61.11%), non-smokers (62.50%), and with histological type corresponding to adenocarcinoma (76.38%). The most frequent EGFR gene mutation was the deletion of exon 19 (65.27%). The majority of patients presented with comorbidities (77.78%), most commonly hypertension. Almost all patients had stage IV NSCLC. Out of the 72 cases, 65 (90.28%) died. The median survival was 9.3 months (95% CI, 7.01-16.93). When comparing the survival curves when using the Log Rank Test, histological type ( $P = 0.01$ ), place of mutation ( $P = 0.06$ ), hemoglobin ( $P = 0.01$ ) and age ( $P = 0.01$ ) were significant associated to overall survival (OS). In multivariate analysis, only age (HR, 1.02; 95% CI, 1-1.04,  $P = 0.009$ ) and hemoglobin (HR, 0.70; 95% CI, 0.55-0.89,  $P = 0.003$ ) remained significant. In conclusion, the median OS of NSCLC patients with positive EGFR gene mutation treated with TKI was 9.3 months. Bivariate and multivariate analysis showed that younger age and a higher hemoglobin level were the most important factors associated with survival.

**Keywords:** Epidermal growth factor receptor mutation, non-small cell lung cancer, tyrosine kinase inhibitors, erlotinib



EXPOSICIÓN ↔ EFECTO Transversales

EXPOSICIÓN ← EFECTO Casos y Controles

EXPOSICIÓN → EFECTO Cohortes

# Estudios Ecológicos

- ▶ Buscan la presencia de una asociación a nivel de grupos poblacionales
- ▶ Ejemplos: Asociación de PBI con niveles de nutrición, carga de enfermedad, etc. Asociación entre prevalencia de hipertensión e ingreso promedio de acuerdo a distritos
- ▶ Falacia ecológica: La asociación a nivel colectivo no necesariamente es la misma a nivel individual.

Mortalidad



Perú

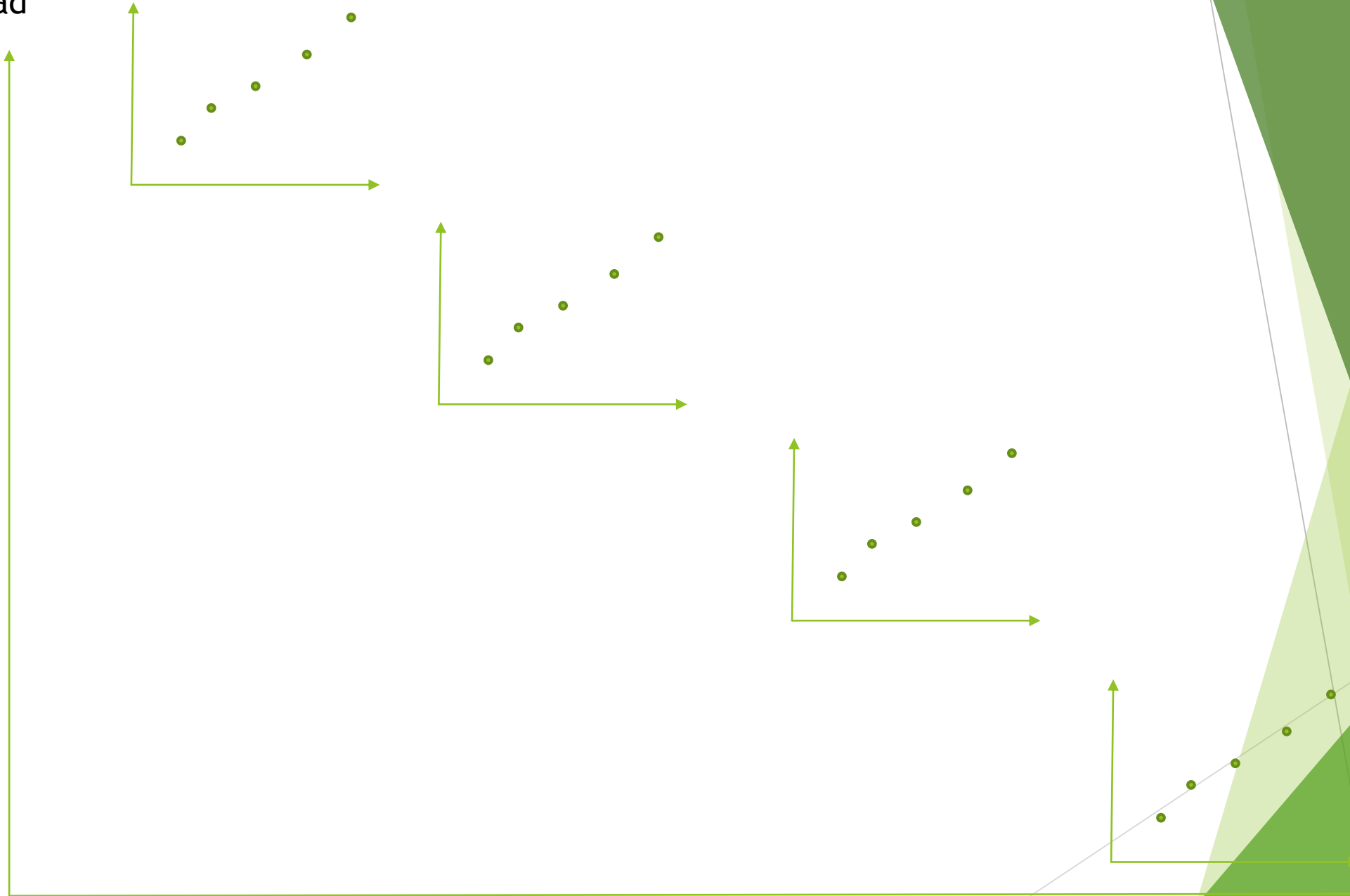
Argentina

Francia

Italia

Consumo  
de OH

Mortalidad



Consumo de OH

# Principales inconvenientes de Estudios Observacionales

**SESGOS:** Desviaciones sistemáticas de la realidad\*

**Sesgo de selección:**

Falta de comparabilidad entre incluidos y no incluidos en estudio (validez externa)

Falta de comparabilidad entre expuestos y no expuestos (validez interna)

**Sesgo de información:** del observador, de “encuestador”, de recuerdo, deseabilidad social, performance, detección, etc

Los sesgos pueden ser controlados en el diseño del estudio

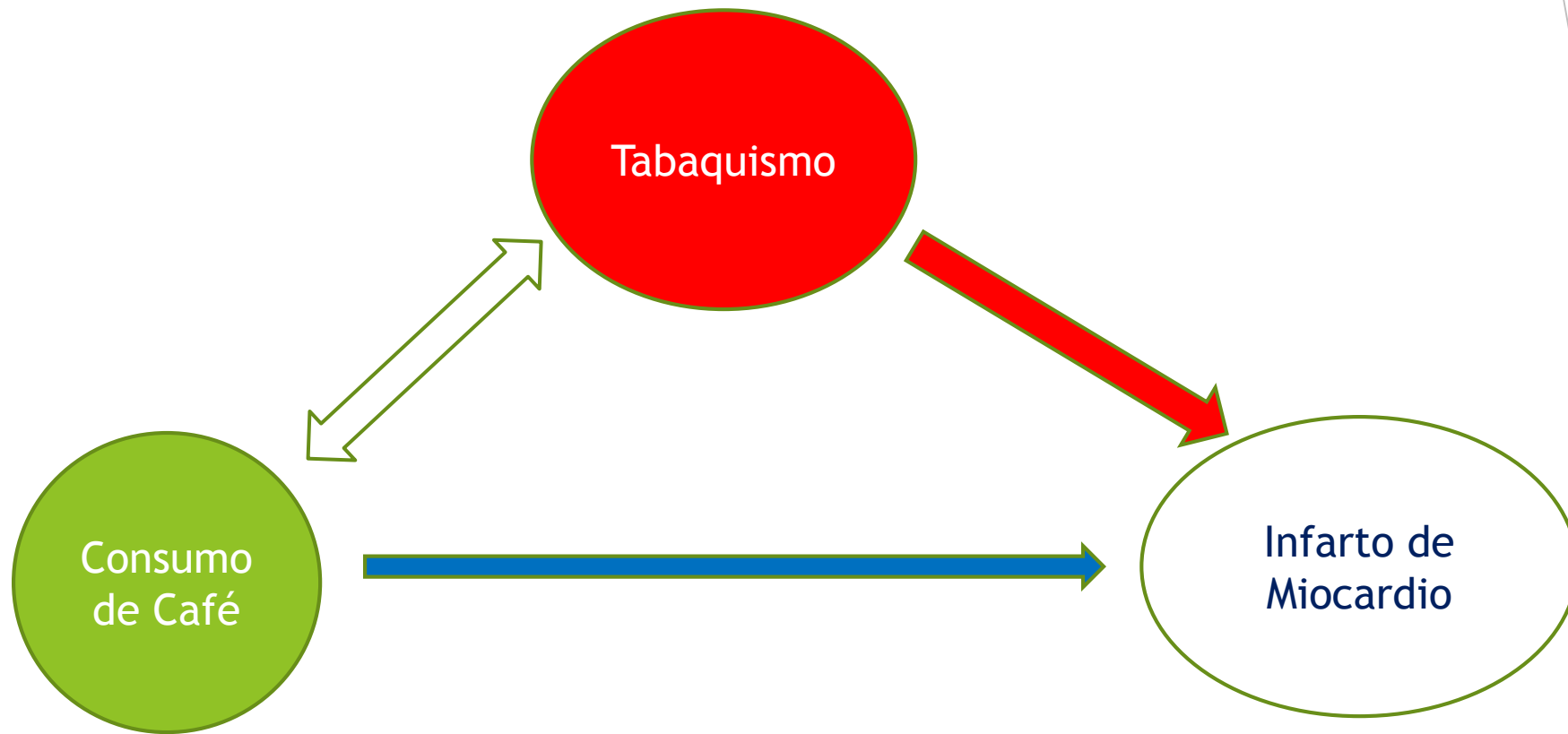
**CONFUSIÓN**

Hallazgo de una asociación inexistente debido a otros factores relacionados a la exposición y al efecto

Puede escapar al control del investigador

# Asociación entre consumo de café e infarto de miocardio

- ▶ Los pacientes consumidores de café presentan una mayor incidencia de infarto de miocardio en una cohorte poblacional



# Evaluación de pruebas diagnósticas

- ▶ ¿Qué es una prueba diagnóstica?

- ▶ Toda evaluación de prueba diagnóstica requiere un ESTÁNDAR de REFERENCIA

# Evaluar UTILIDAD REAL de pruebas ya existentes



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## The validity of cerebrospinal fluid parameters for the diagnosis of tuberculous meningitis<sup>☆</sup>



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Tulia Battaglioli<sup>a</sup>, Roberto Alfonso Accinelli<sup>d,e</sup>, Eduardo Gotuzzo<sup>e,f</sup>, Patrick van der Stuyft<sup>a,g</sup>

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Adenosine deaminase  
Sensitivity and specificity  
Diagnosis  
Neurological

### SUMMARY

**Objectives:** To assess the diagnostic validity of laboratory cerebrospinal fluid (CSF) parameters for discriminating between tuberculous meningitis (TBM) and other causes of meningeal syndrome in high tuberculosis incidence settings.

**Methods:** From November 2009 to November 2011, we included patients with a clinical suspicion of meningitis attending two hospitals in Lima, Peru. Using a composite reference standard, we classified them as definite TBM, probable TBM, and non-TBM cases. We assessed the validity of four CSF parameters, in isolation and in different combinations, for diagnosing TBM: adenosine deaminase activity (ADA), protein level, glucose level, and lymphocytic pleocytosis.

**Results:** One hundred and fifty-seven patients were included; 59 had a final diagnosis of TBM (18 confirmed and 41 probable). ADA was the best performing parameter. It attained a specificity of 95%, a positive likelihood ratio of 10.7, and an area under the receiver operating characteristics curve of 82.1%, but had a low sensitivity (55%). None of the combinations of CSF parameters achieved a fair performance for 'ruling out' TBM.

**Conclusions:** Finding CSF ADA greater than 6 U/l in patients with a meningeal syndrome strongly supports a diagnosis of TBM and permits the commencement of anti-tuberculous treatment.

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# Optimización de pruebas conocidas

Rev Peru Med Exp Salud Publica. 2012; 29(2):223-27.

ORIGINAL BREVE

## DETECCIÓN DE TUBERCULOSIS EN EL SERVICIO DE EMERGENCIA: UTILIDAD DE LA SEGUNDA BACILOSCOPIA REALIZADA EL MISMO DÍA

Gina Tello<sup>1,a</sup>, Martha Ugarte<sup>1,b</sup>, Juan Agapito<sup>1,2,c</sup>, Alonso Soto<sup>3,d</sup>

### RESUMEN

La realización de una baciloscopia el mismo día de la atención del paciente es una estrategia que recientemente ha sido adoptada por la Organización Mundial de la Salud. Nuestro estudio buscó determinar el rendimiento diagnóstico adicional de una segunda baciloscopia tomada en un mismo día en pacientes con síntomas respiratorios, atendidos en el servicio de emergencia de dos hospitales de Lima. Se incluyeron 270 pacientes desde enero a noviembre de 2011, a los cuales se les solicitó dos muestras de esputo con un lapso de dos horas; las muestras fueron procesadas mediante el método de Ziehl Neelsen. La frecuencia de baciloscopias positivas fue del 18,5%. El rendimiento diagnóstico adicional de la segunda baciloscopia fue 20,9%. Considerando la alta frecuencia de tuberculosis diagnosticada por baciloscopia, se sugiere que esta prueba sea incluida de manera rutinaria en las emergencias de los hospitales de Lima Metropolitana.

**Palabras clave:** Tuberculosis; Esputo; Signos y síntomas respiratorios; Perú (Fuente: DeCS BIREME)

# COMPARACIÓN DE LAS FÓRMULAS COCKCROFT-GAULT Y MDRD CON LA DEPURACIÓN DE LA CREATININA ENDÓGENA PARA LA ESTIMACIÓN DE LA FUNCIÓN RENAL EN PACIENTES ADULTOS AMBULATORIOS ATENDIDOS EN UN HOSPITAL DE REFERENCIA PERUANO

*COMPARISON OF THE COCKCROFT-GAULT AND MDRD EQUATIONS WITH THE ENDOGENOUS CREATININE CLEARANCE TO ESTIMATE RENAL FUNCTION IN AMBULATORY ADULT PATIENTS TREATED IN A PERUVIAN REFERENCE HOSPITAL*

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Rev Nefrol Dial Traspl. 2019; 39 (3): 159-66

# Desarrollo de pruebas diagnósticas

128

## **Development of a Clinical Scoring System for the Diagnosis of Smear-Negative Pulmonary Tuberculosis**

**Alonso Soto<sup>1,2</sup>, Lely Solari<sup>2</sup>, Juan Agapito<sup>2</sup>, Carlos Acuna-Villaorduna<sup>2</sup>,  
Marie-Laurence Lambert<sup>2</sup>, Eduardo Gotuzzo<sup>4</sup> and Patrick Van der Stuyff<sup>2</sup>**

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**This study developed a clinical score based on clinical and radiographic data for the diagnosis of smear-negative pulmonary tuberculosis (SNPT). SNPT was defined as a positive culture in Ogawa in a patient with two negative sputum smears. Data from patients admitted to the emergency ward with respiratory symptoms and negative acid-fast bacilli (AFB) smears was analyzed by means of logistic regression to develop the predictive score. Two hundred and sixty two patients were included. Twenty patients had SNPT. The variables included in the final model were hemoptysis, weight loss, age > 45 years old, productive cough, upper-lobe infiltrate, and miliary infiltrate. With those, a score was constructed. The score values ranged from -2 to 6. The area under the curve for the ROC curve was 0.83 (95% CI 0.74-0.90). A score of value 0 or less was associated with a sensitivity of 93% and a score of more than 4 points was associated with a specificity of 92% for SNPT. Fifty-two point twenty-nine percent of patients had scores of less than one or more than four, what provided strong evidence against and in favor, respectively, for the diagnosis of SNPT. The score developed is a cheap and useful clinical tool for the diagnosis of SNPT and can be used to help therapeutic decisions in patients with suspicion of having SNPT.**

**Key-Words:** Tuberculosis, pulmonary, regression analysis, scoring methods.

# Evaluación de Reglas de predicción clínica (sistemas de puntaje, scores)

## Validation of a Clinical-Radiographic Score to Assess the Probability of Pulmonary Tuberculosis in Suspect Patients with Negative Sputum Smears

Alonso Soto<sup>1\*</sup>, Lely Solari<sup>2</sup>, Javier Díaz<sup>3</sup>, Alberto Mantilla<sup>1</sup>, Francine Matthys<sup>2</sup>, Patrick van der Stuyft<sup>2</sup>

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### Abstract

**Background:** Clinical suspects of pulmonary tuberculosis in which the sputum smears are negative for acid fast bacilli represent a diagnostic challenge in resource constrained settings. Our objective was to validate an existing clinical-radiographic score that assessed the probability of smear-negative pulmonary tuberculosis (SNPT) in high incidence settings in Peru.

**Methodology/Principal Findings:** We included in two referral hospitals in Lima patients with clinical suspicion of pulmonary tuberculosis and two or more negative sputum smears. Using a published but not externally validated score, patients were classified as having low, intermediate or high probability of pulmonary tuberculosis. The reference standard for the diagnosis of tuberculosis was a positive sputum culture in at least one of 2 liquid (MGIT or Middlebrook 7H9) and 1 solid (Ogawa) media. Prevalence of tuberculosis was calculated in each of the three probability groups. 684 patients were included. 184 (27.8%) had a diagnosis of pulmonary tuberculosis. The score did not perform well in patients with a previous history of pulmonary tuberculosis. In patients without, the prevalence of tuberculosis was 5.1%, 31.7% and 72% in the low, intermediate and high probability group respectively. The area under the ROC curve was 0.76 (95% CI 0.72–0.80) and scores  $\geq 6$  had a positive LR of 10.9.

**Conclusions/Significance:** In smear negative suspects without previous history of tuberculosis, the clinical-radiographic score can be used as a tool to assess the probability of pulmonary tuberculosis and to guide the decision to initiate or defer treatment or to requesting additional tests.

# Evaluación de Algoritmos existentes

Tropical Medicine and International Health

doi:10.1111/j.1365-3156.2010.02715.x

VOLUME 16 NO 4 PP 424-430 APRIL 2011

## Performance of an algorithm based on WHO recommendations for the diagnosis of smear-negative pulmonary tuberculosis in patients without HIV infection

Alonso Soto<sup>1</sup>, Lely Solari<sup>2</sup>, Eduardo Gotuzzo<sup>3</sup>, Roberto Acinelli<sup>4</sup>, Dante Vargas<sup>1</sup> and Patrick Van der Stuyft<sup>5</sup>

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### Summary

**OBJECTIVE** To evaluate the performance of an algorithm based on WHO recommendations for diagnosis of smear-negative pulmonary tuberculosis in HIV-negative patients

		Enfermedad		
		Presente	Ausente	
Test	Positivo	Verdaderos Positivos	Falsos Positivos	Total positivos
	Negativo	Falsos Negativos	Verdaderos Negativos	Total negativos
		Enfermos	Sanos	Total

# Estudios de Intervención

The background features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. These shapes are primarily located on the right side of the slide, creating a modern, layered effect. The text 'Estudios de Intervención' is positioned on the left side of the slide in a clean, sans-serif font.

- ▶ Intervención en la que el investigador no tiene posibilidad de controlar la intervención (habitualmente intervenciones demostradas en otros escenarios)  
**:Estudios quasi-experimentales**
- ▶ Intervención en la cual existe una comparación (grupo control) con un grupo de referencia comparables bajo condiciones de intervención y mediadas estandarizadas:  
Estudio experimental
- ▶ Los estudios experimentales en humanos se denominan  
Ensayos Clínicos

# Estudios quasi-experimentales

- ▶ Habitualmente del tipo “antes y después.”
- ▶ Obtención de indicadores previos a la intervención (línea de base) y posteriores a la intervención.

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Línea de base

Intervención

Post-intervención

# Ensayos Clínicos

- ▶ **Ensayo clínico aleatorizado:** los controles se distribuyen de manera aleatoria
- ▶ **Ensayo clínico controlado** se utiliza un grupo control (que no recibe la intervención).
- ▶ **Enmascaramiento (ciego):** implica no tener conocimiento del tratamiento recibido
  - ▶ Ciego simple : el paciente no conoce el tratamiento recibido
  - ▶ Doble ciego : ni el paciente ni el investigador conocen el tratamiento recibido
  - ▶ Puede extenderse el concepto al evaluador de resultados e incluso al encargado del análisis.

Reclutamiento de  
participantes

Verificación de criterios  
inclusión/exclusión  
Consentimiento informado

# Aleatorización

Intervención  
(Fármaco/Dispositivo  
biomédico/ etc)

Control (mejor tratamiento  
disponible o placebo de no  
existir)

Enmascaramiento

Resultado  
(Outcome/End-point)  
presente

Resultado  
(Outcome/End-point)  
ausente

Resultado  
(Outcome/End-point)  
presente

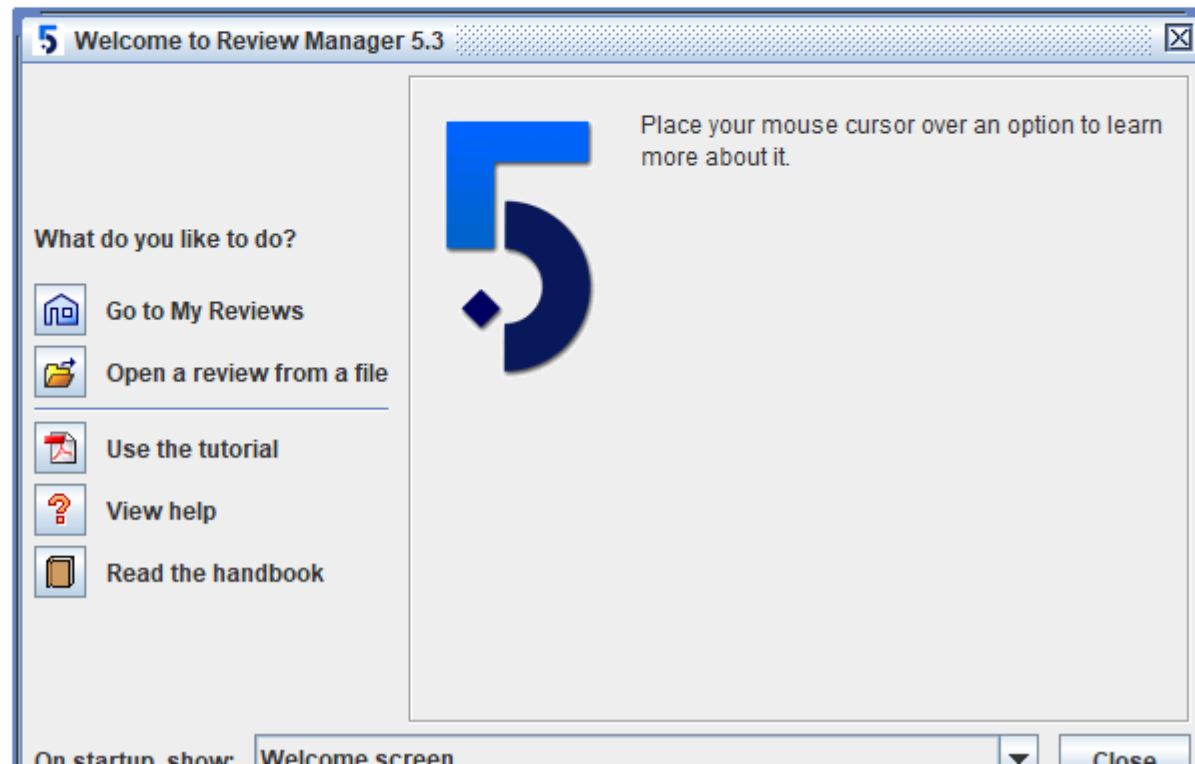
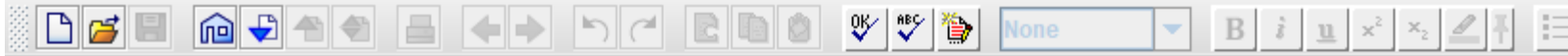
Resultado  
(Outcome/End-point)  
ausente

Intención a tratar!

# Revisiones Sistemáticas

5 Review Manager 5.3

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# Pirámide de Evidencias

