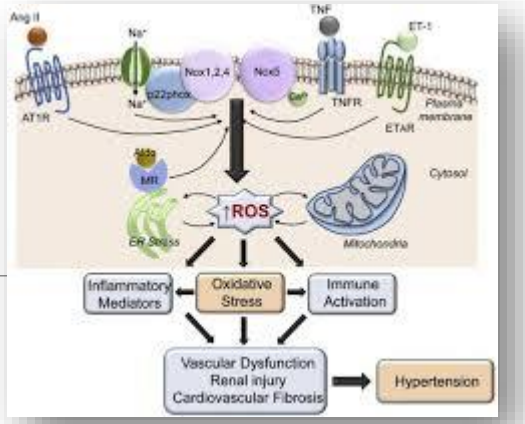
"There's a flaw in your experimental design.
All the mice are scorpios."

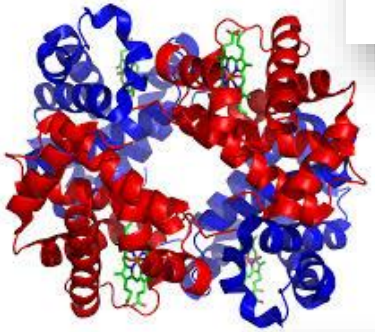
Diseño de estudios en biomedicina y biotecnología

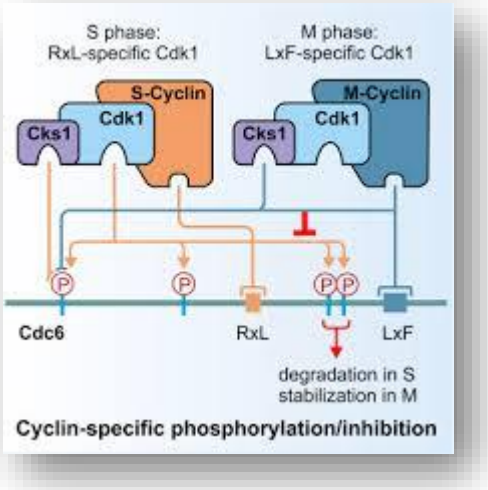
La investigación en biomedicina y biotecnología



Básica

- Mecanismos moleculares responsables de situaciones patológicas
  - Ciclo celular y cáncer
  - Estrés oxidativo y envejecimiento
- Desarrollo de tratamientos
  - Mutagénesis dirigida
  - Dinámica molecular
  - Modelos matemáticos
  - Farmacología experimental
  - Química orgánica

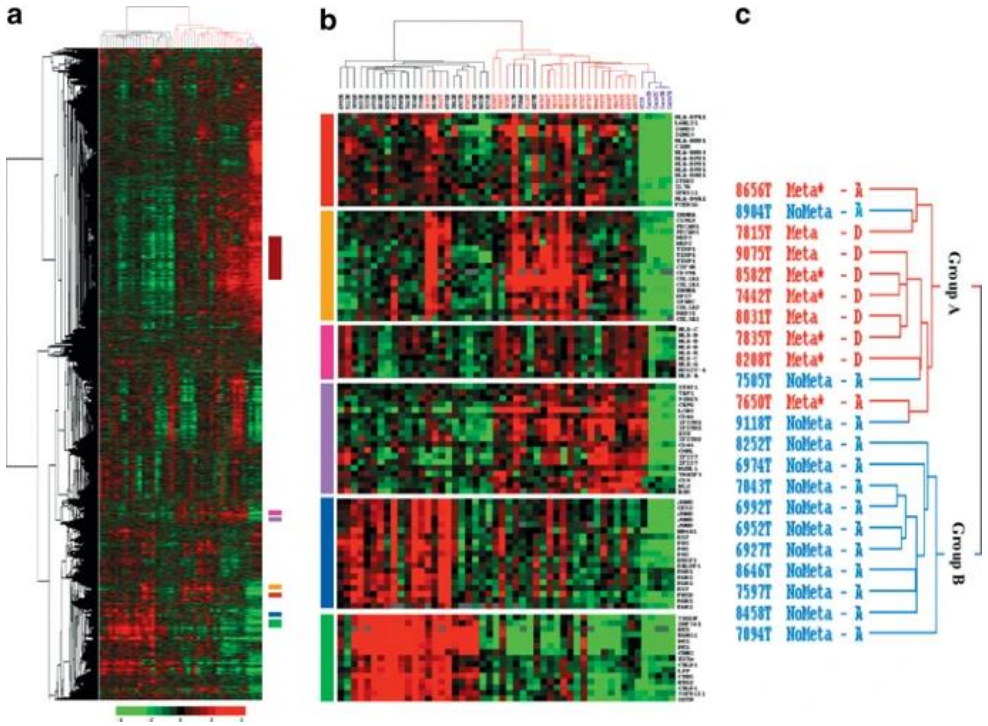




La investigación en biomedicina y biotecnología

Básica

- Identificación de procesos patológicos
  - Biología celular
  - Anatomía patológica
  - Fisiología
  - Análisis genético



La investigación en biomedicina

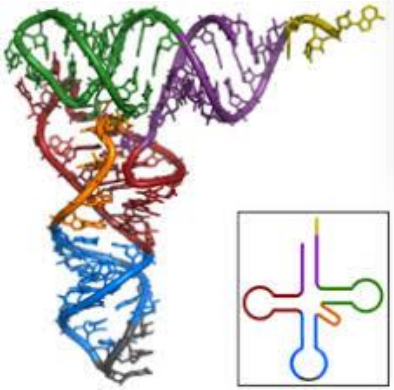
Clínico-epidemiológica

- Descripción de procesos patológicos
- Asociación síntoma-enfermedad
- Ensayos clínicos
  - Evaluación de tratamientos
  - Ensayos en grupos de enfermos
  - Seguimiento en la población
- Análisis epidemiológico
  - Seguimiento de enfermedades de declaración obligatoria
  - Procesos epidemiológicos (p.e. HIV)
  - Modelos matemáticos

La investigación en biotecnología

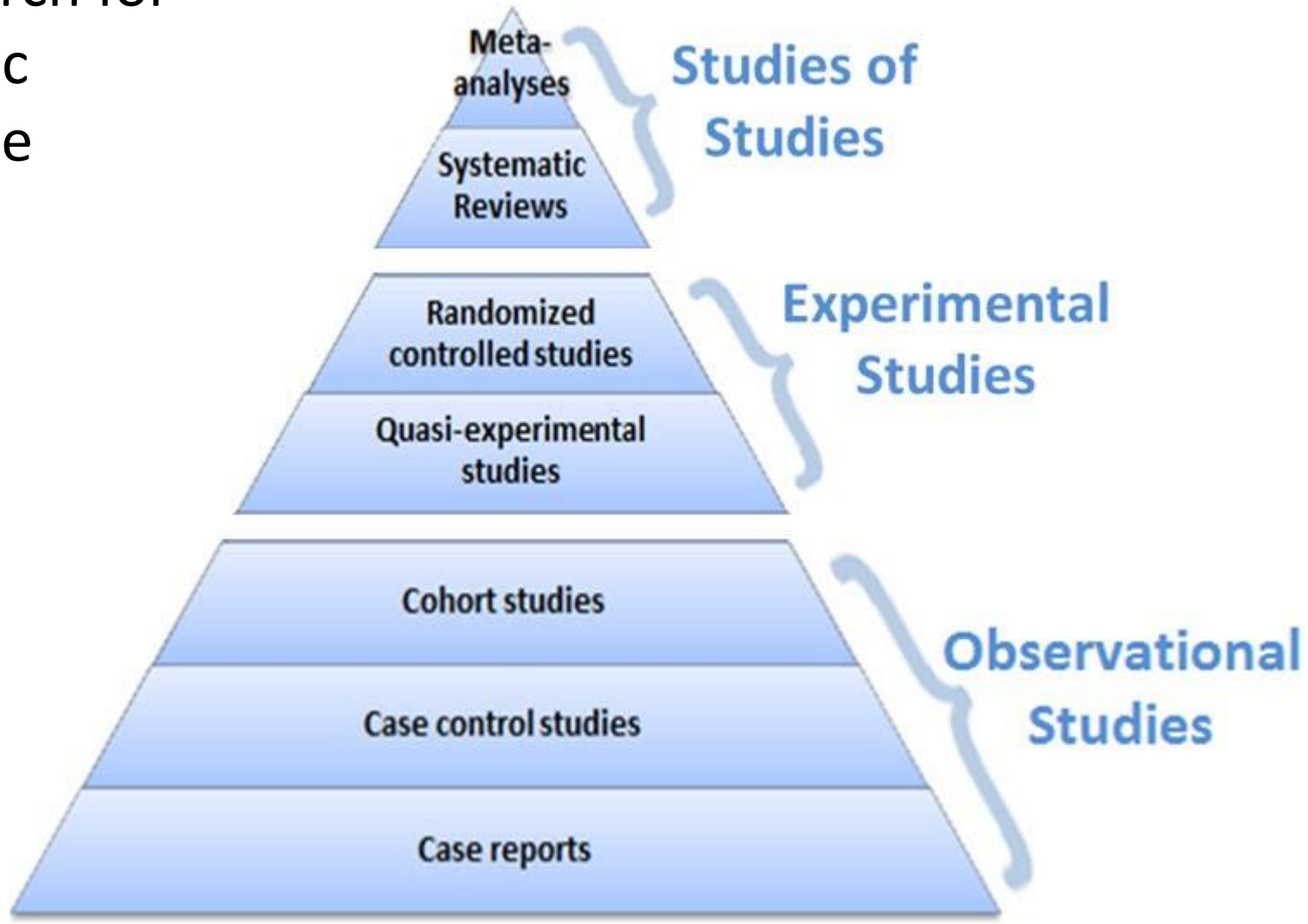
Diseño de nuevos fármacos
- Identificación de dianas terapéuticas
- Modelos de vías metabólicas
- Ensayos de farmacodinámica
- Evaluación de la efectividad

Procesos industriales (fermentación)
- Optimización de procesos
- Modelos predictivos de rendimiento
- Evaluación de factores críticos



Biología sintética
- Análisis bioinformático
- Métodos genómicos
- Evaluación de estados metabólicos

The search for scientific evidence



Types of studies

Observational
- Descriptive
- Cross-sectional
- Cohort

Experimental
- Randomized controlled trial

Studies of studies
- Systematic reviews
- Meta-analyses

Increasing level of evidence

Confounding: risk factors don't happen in isolation, except in a controlled experiment.

Principales tipos de diseños

Estudios experimentales

- El experimentador diseña un estudio con el objetivo de **controlar** al máximo las fuentes de variabilidad.
- Las condiciones del experimento están especificadas por el experimentador.

Estudios observacionales

- En general, la información se obtiene en condiciones donde es muy difícil controlar las fuentes de variabilidad.

Principales tipos de diseños Ejemplos

Experimentales

- Ensayos clínicos
  - Desarrollo de nuevos fármacos, comparación de tratamientos, bioequivalencia entre tratamientos, estudios dosis-respuesta,…
- Requieren un planteamiento cuidadoso
- El experimentador controla las condiciones
- Establecer causa-efecto

Observacionales

- Encuestas de salud, epidemiología, estudios retrospectivos, estadísticas de mortalidad,…
- Se recoge información sin cambiar las condiciones de la población
- Es difícil establecer relaciones de causa-efecto

Estudios experimentales
Ejemplos

Establecer el efecto de un tratamiento de nueva síntesis.

- Se escogen individuos de entre los que padecen una cierta enfermedad. La selección se realiza en base a unos criterios de inclusión en el estudio.
- Se dividen **al azar** los sujetos en distintos grupos de estudio, en función de las condiciones que se quieran evaluar. Por ejemplo, un grupo control y un grupo de tratamiento.
- Las condiciones de cada grupo se definen por el experimentador: Grupo control con placebo, Grupo experimental tratado con el nuevo fármaco.

Estudios experimentales
Ejemplos

Determinar el efecto de la temperatura y la humedad en el crecimiento de mohos en alimentos.

- Decidir la temperatura y la humedad a la que se realizaran los experimentos.
- Establecer una pauta para inocular los cultivos.
- Determinar una medida de crecimiento.
- Las diferencias de crecimiento deben ser atribuibles a la variación de temperatura y humedad. Por lo tanto, cualquier otro factor debería estar controlado.

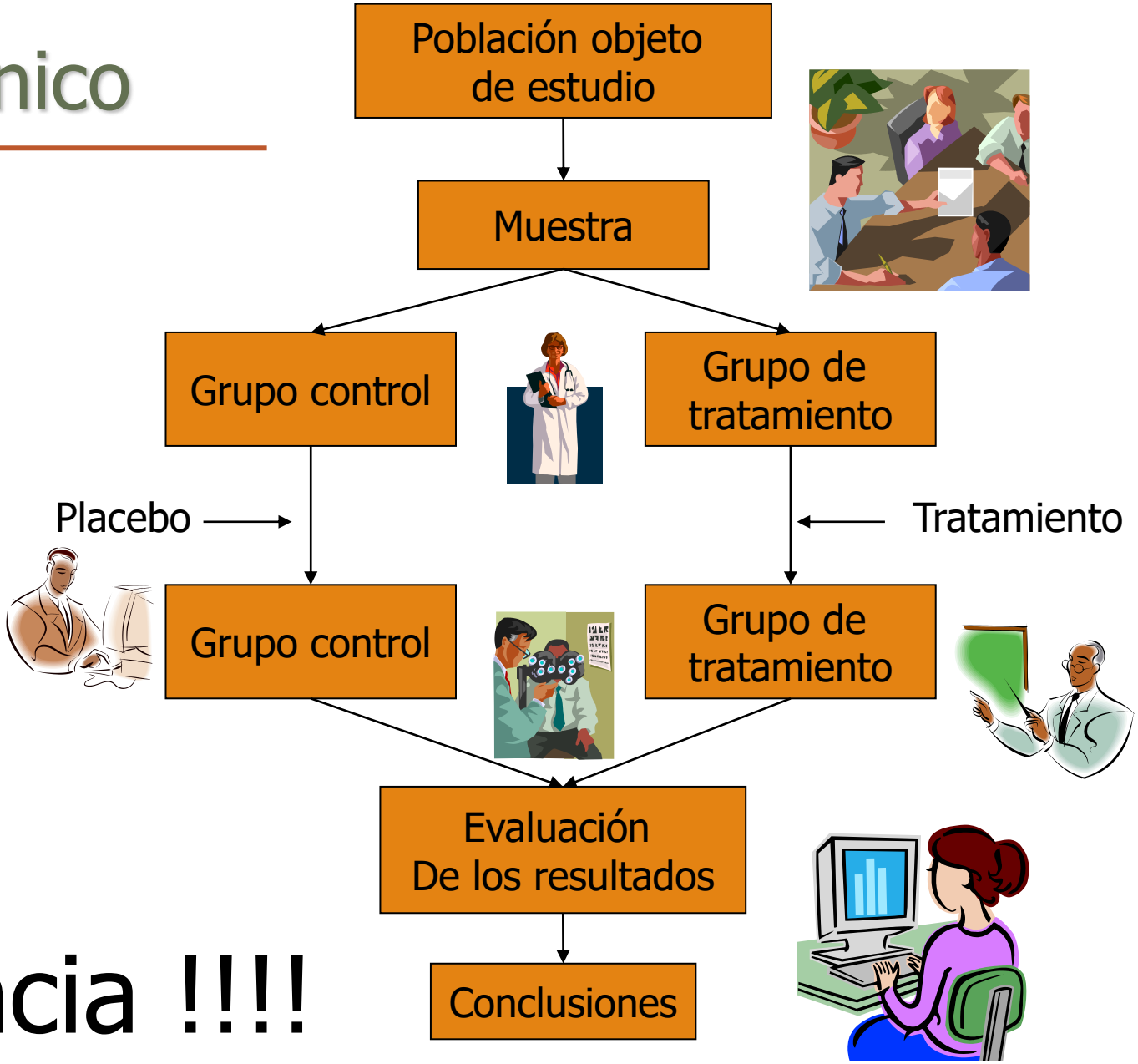
Ensayo clínico (estudio experimental)

- Características básicas
  - Distintos grupos experimentales según el tratamiento
  - Grupos equilibrados (***asignación al azar***)
  - Control de las condiciones por parte del experimentador (**controlar factores de confusión**)
  - Protocolo experimental (**estandarizar métodos**)
  - Evaluación objetiva de resultados (análisis estadístico)

Ensayo clínico

La fama !!!!

Ensayo clínico



La ciencia !!!!

Ensayo clínico
Aspectos prácticos fundamentales

Grupos experimentales al azar

Diseño a doble ciego

- El paciente desconoce a qué tratamiento está sometido
- El médico evalúa el estado de salud desconociendo el tratamiento

La evaluación de resultados debe hacerse lo más objetiva posible: p.e. se compara el grupo 1 y el grupo 2 desconociendo qué grupo es el control y qué grupo es el de tratamiento

Randomized clinical trials

Considered the **gold standard** of study design

Advantages

- Randomization minimizes confounding.
- Blinding minimizes bias.

Limitations

- Expensive
- Can only look at short-term outcomes.
- Not always ethical to randomize
- Results may not be generalizable

Comparison of upper gastrointestinal toxicity of Vioxx and Naproxen in patients with rheumatoid arthritis. Researchers randomly assigned 8076 patients with rheumatoid arthritis to receive either Vioxx or Naproxen (non-steroidal anti-inflammatory) twice daily. The study was double blind. The primary end point was confirmed clinical upper gastrointestinal events (such as ulcers and bleeding). (Bombardier et al. NEJM 2000; 343: 1520-8)

Ways to avoid or control for confounding

During the design phase: randomize or match

In the analysis phase: use multivariate regression to statistically "adjust for" confounders

- Statistical adjustment is not a panacea; you cannot control for all confounders and there is always "residual" confounding

1: Lancet 2002 Aug 17;360(9332):528

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

Rifapentine and isoniazid once a week versus rifampicin and isoniazid twice a week for treatment of drug-susceptible pulmonary tuberculosis in HIV-negative patients: a randomised clinical trial.

Background Rifapentine has a long half-life in serum, which suggests a possible treatment once a week for tuberculosis. We aimed to compare rifapentine and isoniazid once a week with rifampicin and isoniazid twice a week.Methods We did a randomised, multicentre, open-label trial in the USA and Canada of HIV-negative people with drug-susceptible pulmonary tuberculosis who had completed 2 months of a 6-month treatment regimen. We randomly allocated patients directly observed treatment with either 600 mg rifapentine plus 900 mg isoniazid once a week or 600 mg rifampicin plus 900 mg isoniazid twice a week. Primary outcome was failure/relapse. Analysis was by intention to treat.Findings 1004 patients were enrolled (502 per treatment group). 928 successfully completed treatment, and 803 completed the 2-year 4-month study. Crude rates of failure/relapse were 46/502 (9.2%) in those on rifapentine once a week, and 28/502 (5.6%) in those given rifampicin twice a week (relative risk 1.64, 95% CI 1.04-2.58, p=0.04). By proportional hazards regression, five characteristics were independently associated with increased risk of failure/relapse: sputum culture positive at 2 months (hazard ratio 2.8, 95% CI 1.7-4.6); cavitation on chest radiography (3.0, 1.6-5.9); being underweight (3.0, 1.8-4.9); bilateral pulmonary involvement (1.8, 1.0-3.1); and being a non-Hispanic white person (1.8, 1.1-3.0). Adjustment for imbalances in 2-month culture and cavitation diminished the association of treatment group with outcome (1.34; 0.83-2.18; p=0.23). Of participants without cavitation, rates of failure/relapse were 6/210 (2.9%) in the once a week group and 6/241 (2.5%) in the twice a week group (relative risk 1.15; 95% CI 0.38-3.50; p=0.81). Rates of adverse events and death were similar in the two treatment groups.Interpretation Rifapentine once a week is safe and effective for treatment of pulmonary tuberculosis in HIV-negative people without cavitation on chest radiography. Clinical, radiographic, and microbiological data help to identify patients with tuberculosis who are at increased risk of failure or relapse when treated with either regimen.

PMID: 12241657 [PubMed - as supplied by publisher]

Stroke 2002 Jan;33(1):130-4

Related Articles, NEW Links

Comment in:

- Stroke. 2002 Jan;33(1):134-5.

Acetaminophen for altering body temperature in acute stroke: a randomized clinical trial.

Kasner SE, Wein T, Piriyawat P, Villar-Cordova CE, Chalela JA, Krieger DW, Morgenstern LB, Kimmel SE, Grotta JC.

Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia 19104, USA. kasner@mail.med.upenn.edu

BACKGROUND AND PURPOSE: Mild alterations in temperature have prominent effects on ischemic cell injury and stroke outcome. Elevated core body temperature (CBT), even if mild, may exacerbate neuronal injury and worsen outcome, whereas hypothermia is potentially neuroprotective. The antipyretic effects of acetaminophen were hypothesized to reduce CBT. METHODS: This was a randomized, controlled clinical trial at 2 university hospitals. Patients were included if they had stroke within 24 hours of onset of symptoms, National Institutes of Health Stroke Scale (NIHSS) score > or =5, initial CBT <3 8.5 degrees C, and white blood cell count < 12 600 cells/mm(3); they were excluded if they had signs of infection, severe medical illness, or contraindication to acetaminophen. CBT was measured every 30 minutes. Patients were randomized to receive acetaminophen 650 mg or placebo every 4 hours for 24 hours. The primary outcome measure was mean CBT during the 24-hour study period; the secondary outcome measure was the change in NIHSS. RESULTS: Thirty-nine patients were randomized. Baseline CBT was the same: 36.96 degrees C for acetaminophen versus 36.95 degrees C for placebo (P=0.96). During the study period, CBT tended to be lower in the acetaminophen group (37.13 degrees C versus 37.35 degrees C), a difference of 0.22 degrees C (95% CI, -0.08 degrees C to 0.51 degrees C; P=0.14). Patients given acetaminophen tended to be more often hypothermic <36.5 degrees C (OR, 3.4; 95% CI, 0.83 to 14.2; P=0.09) and less often hyperthermic >37.5 degrees C (OR, 0.52; 95% CI, 0.19 to 1.44; P=0.22). The change in NIHSS scores from baseline to 48 hours did not differ between the groups (P=0.93). CONCLUSIONS: Early administration of acetaminophen (3900 mg/d) to afebrile patients with acute stroke may result in a small reduction in CBT. Acetaminophen may also modestly promote hypothermia <36.5 degrees C or prevent hyperthermia >37.5 degrees C. These effects are unlikely to have robust clinical impact, and alternative or additional methods are needed to achieve effective thermoregulation in stroke patients.

Investigación en biomedicina

Estudios observacionales

- Asociación síntoma-enfermedad
- Estado de salud de la población
- Encuestas de servicios de salud
- Estudios poblacionales
- Seguimiento de vacunaciones
- Estadísticas de mortalidad

Estudio observacional

Cierto tipo de pacientes muestran una mortalidad elevada por efecto del virus de la gripe A.

- ¿Qué factores pueden ser responsables de esta situación? ¿Pueden establecerse diferencias debidas a factores genéticos?
- En esta situación, analizamos retrospectivamente a un conjunto de pacientes para establecer la posible relación entre el problema y las causas.
- Debemos establecer un grupo de comparación. Por ejemplo las personas infectadas de gripe A que cursan con una afectación benigna.

Investigación en biomedicina

Estudios observacionales

- Estudio de casos y controles
  - Seleccionamos la muestra en función de la presencia (**casos**) o ausencia (**controles**) de una determinada característica y queremos investigar cual es la posible causa.

Case-Control Studies

Sample on disease status and ask retrospectively about exposures

Advantages: Efficient for rare diseases and outbreak situations

Limitations

- Getting appropriate controls is tricky.
- Recall bias
- Confounding
- The risk factor may have come after the disease

- Early case-control studies among AIDS cases and matched controls indicated that AIDS was transmitted by sexual contact or blood products.
- In 1982, an early case-control study matched AIDS cases to controls and found a large, positive association between amyl nitrites ("poppers") and AIDS (Marmor et al. NEJM, 1982). This is an example of confounding.

1: Lancet 2002 Aug 31;360(9334):678

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

Contacts with varicella or with children and protection against herpes zoster in adults: a case-control study.

Thomas S, Wheeler J, Hall A.

Infectious Disease Epidemiology Unit, London School of Hygiene and Tropical Medicine, Keppel Street, WC1E 7HT, London, UK

Background Whether exogenous exposure to varicella-zoster-virus protects individuals with latent varicella-zoster virus infection against herpes zoster by boosting immunity is not known. To test the hypothesis that contacts with children increase exposure to varicella-zoster virus and protect latently infected adults against zoster, we did a case-control study in south London, UK.Methods From 22 general practices, we identified patients with recently diagnosed zoster, and control individuals with no history of zoster, matched to patients by age, sex, and practice. Participants were asked about contacts with people with varicella or zoster in the past 10 years, and social and occupational contacts with children as proxies for varicella contacts. Odds ratios were estimated with conditional logistic regression.Findings Data from 244 patients and 485 controls were analysed. On multivariable analysis, protection associated with contacts with a few children in the household or via childcare seemed to be largely mediated by increased access to children outside the household. Social contacts with many children outside the household and occupational contacts with ill children were associated with graded protection against zoster, with less than a fifth the risk in the most heavily exposed groups compared with the least exposed. The strength of protection diminished after controlling for known varicella contacts; the latter remained significantly protective (odds ratio 0.29 [95% CI 0.10-0.84] for those with five contacts or more).Interpretation Re-exposure to varicella-zoster virus via contact with children seems to protect latently infected individuals against zoster. Reduction of childhood varicella by vaccination might lead to increased incidence of adult zoster. Vaccination of the elderly (if effective) should be considered in countries with childhood varicella vaccination programmes.

PMID: 12241874 [PubMed - in process]

Investigación en biomedicina

Estudios observacionales

- Estudio de cohortes
  - Seleccionamos un grupo de individuos en función de la exposición a un determinado factor (**causa**) y queremos evaluar su influencia en la aparición de una determinada enfermedad (**efecto**).

Prospective cohort study

Measure risk factors on people who are disease-free at baseline; then follow them over time and calculate risks or rates of developing disease

Advantages:

- Exposures are measured prior to outcomes!
- Can study multiple outcomes

Limitations

- Time and money!
- Confounding
- Loss to follow-up

The Framingham Heart Study enrolled 5209 residents of Framingham, MA, aged 28 -62 in 1948. Researchers measured their health and lifestyle factors (blood pressure, weight, exercise, etc.) and followed them for decades to determine the occurrence of heart disease. The study continues today, tracking the kids and grandkids of the original cohort.

Retrospective cohort study

Conceptually similar to a prospective cohort study, but the cohort is assembled after outcomes have occurred using stored data.

Advantages

- Exposure data were collected before outcomes occurred.
- Cheaper and faster than prospective designs

Limitation: Data quality may be limited

Mortality in former Olympic athletes: Using the Sports Reference database, researchers identified a cohort of 9889 athletes who participated in the Olympic Games between 1896 and 1936 and were born before 1910. They used the database to find dates of death for these athletes. Then they compared the mortality rates of athletes in different types of sports (BMJ 2012; 345: e7456.)

1: Lancet 2002 Aug 3;360(9330):368

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

Cardiovascular status of infants and children of women infected with HIV-1 (P(2)C(2) HIV): a cohort study.

Lipshultz S, Easley K, Orav E, Kaplan S, Starc T, Bricker J, Lai W, Moodie D, Sopko G, Schluchter M, Colan S.

Division of Pediatric Cardiology, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

Background Data from cross-sectional and short-term longitudinal studies have suggested that children infected with HIV-1 might have cardiovascular abnormalities. We aimed to investigate this hypothesis in a long-term cohort study.Methods We measured cardiovascular function every 4-6 months for up to 5 years in a birth cohort of 600 infants born to women infected with HIV-1. We included 93 infants infected with HIV-1 and 463 uninfected infants (internal controls) from the same cohort. We also included a cross-sectionally measured comparison group of 195 healthy children born to mothers who were not infected with HIV-1 (external controls).Findings Children infected with HIV-1 had a significantly higher heart rate at all ages (mean difference 10 bpm, 95% CI 8-13) than internal controls. At birth, both cohort groups of children had similar low left ventricular (LV) fractional shortening. At 8 months, fractional shortening was similar in internal and external controls, whereas in children infected with HIV-1, fractional shortening remained significantly lower than in controls for the first 20 months of life (mean difference from internal controls at 8 months 3.7%, 2.3-5.1). LV mass was similar at birth in both cohort groups, but became significantly higher in children with HIV-1 from 4-30 months (mean difference 2.4 g at 8 months, 0.9-3.9).Conclusions Vertically-transmitted HIV-1 infection is associated with persistent cardiovascular abnormalities identifiable shortly after birth. Irrespective of their HIV-1 status, infants born to women infected with HIV-1 have significantly worse cardiac function than other infants, suggesting that the uterine environment has an important role in postnatal cardiovascular abnormalities.

PMID: 12241776 [PubMed - in process]

Investigación en biomedicina

Estudios observacionales

- Estudio transversal
  - Seleccionamos un grupo de individuos y se recoge la información acerca de las características de interés, p.e. una encuesta de salud.
- Ejemplos:
  - Realizamos una encuesta para determinar el grado de satisfacción de un determinado colectivo profesional respecto de sus condiciones laborales.
  - Comparamos la incidencia de una determinada enfermedad entre distintas comunidades.

Cross-sectional (prevalence) studies

Measure prevalence of the event (disease) and exposure on a random sample of the population of interest at one time point

Advantages: Cheap and easy!

Limitations

- Correlation does not imply causation
- Cannot determine what came 1st
- Confounding

Researchers measured the prevalence of coronary artery calcification (atherosclerosis) and the prevalence of depressive symptoms in a large cohort of elderly men and women in Rotterdam (n=1920). (Tiemeier et al. Arch Gen Psychiatry, 2004).

1: BMJ 2002 Aug 31;325(7362):472

Related Articles, NEW Links

Consultation length in general practice: cross sectional study in six European countries.

Deveugele M, Derese A, van den Brink-Muinen A, Bensing J, De Maeseneer J.

Department of General Practice and Primary Health Care, Ghent University, B 9000 Ghent, Belgium. myriam.deveugele@rug.ac.be

OBJECTIVES: To compare determinants of consultation length discussed in the literature with those found in consultations with general practitioners from different European countries; to explore the determinants of consultation length, particularly the effect of doctors' and patients' perceptions of psychosocial aspects. DESIGN: Analysis of videotaped consultations of general practitioners from the Eurocommunication study and of questionnaires completed by doctors and by patients. SETTING: General practices in six European countries. PARTICIPANTS: 190 general practitioners and 3674 patients. RESULTS: In a multilevel analysis with three levels (country, general practitioner, and patient), country and doctor variables contributed a similar amount to the total variance in consultation length (23% and 22%, respectively) and patient variables accounted for 55% of the variance. The variables used in the multilevel analysis explained 25% of the total variation. The country in which the doctor practised, combined with the doctors' variables, was as important for the variance in consultation length as the variation between patients. Consultations in which psychosocial problems were considered important by the doctor and the patient lasted longer than consultations about biomedical problems only. The doctor's perception had more influence in this situation than the patient's. Consultation length is influenced by the patients' sex (women got longer consultations), whether the practice was urban or rural, the number of new problems discussed in the consultation (the more problems the longer the consultation), and the patient's age (the older the patient the longer the consultation). As a doctor's workload increased, the length of consultations decreased. The general practitioner's sex or age and patient's level of education were not related to the length of consultation. CONCLUSION: Consultation length is determined by variables related to the doctor and the doctor's country as well as by those related to patients. Women consulting in an urban practice with problems perceived as psychosocial have longer consultations than other patients.

Publication Types:

- Multicenter Study

Algunos conceptos básicos

Variable: Cada una de las características que se pueden medir en los individuos de un estudio.

- Peso, Altura, Nivel de Colesterol, Edad.
- Número de hijos, Número de gánglios infectados.
- Diámetro de crecimiento de un cultivo.
- Velocidad máxima de crecimiento de un cultivo.

Factor: Cada una de las posibles causas de variabilidad en un estudio:

- Género: Hombre/Mujer, Edad, Temperatura, Humedad, etc.

Factores y variables

En general, nuestro objetivo será el de explicar el comportamiento de ciertas variables en relación a los factores que se consideren en el estudio.

- La humedad y la temperatura como factores que determinan el crecimiento de los mohos.
- El género y la edad como factores que explican la variación de colesterol en sangre.
- La exposición a determinados agentes tóxicos como causa (factor) que determina la aparición de procesos cancerosos.

Factores y variables

- Variación del colesterol con la edad.
- Variación del colesterol con la edad y el género.
- Variación de la mortalidad cardiovascular en función del nivel de colesterol.
- Variación de la mortalidad cardiovascular en hombres y mujeres en función del nivel de colesterol.
- Variación de la mortalidad cardiovascular en función del nivel de colesterol y la hipertensión.
- ¿Cuáles son los factores de riesgo en mortalidad coronaria?

¿Qué valor de colesterol debemos esperar en una persona sana?

¿Qué es una persona sana?

¿Cómo se determina el colesterol?

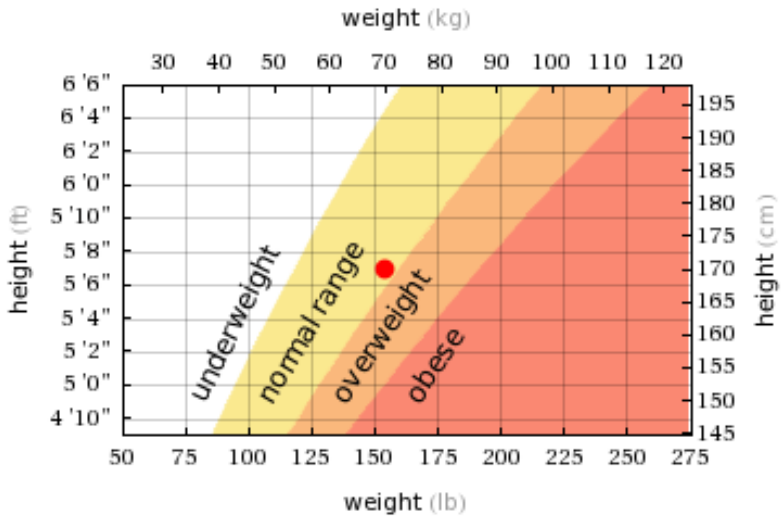
¿Cómo vamos a considerar los distintos factores que pueden hacer variar el nivel de colesterol?

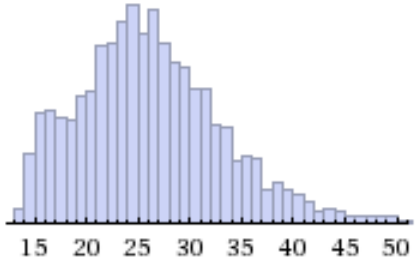
El concepto de distribución es fundamental

Distribución del índice de masa corporal

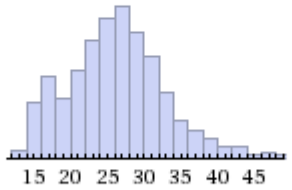
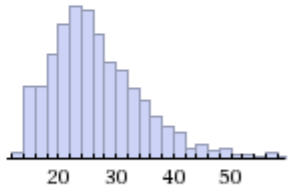
$$BMI = \frac{Weight(Kg)}{Height^2(m)}$$

$$BMI = \frac{75.5}{1.68^2} = 26.6$$



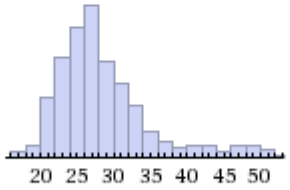
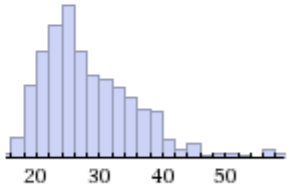
95% reference range	(14.7 to 44)
±1σ range	(18.9 to 34)
distribution	
data sample size	8949 people

(data from NHANES 2006 study, weighted for USA demographics)

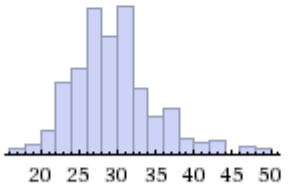
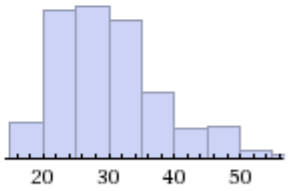
	male	female
95% reference range	(14.8 to 42)	(14.7 to 46)
±1σ range	(19.2 to 33)	(18.6 to 35)
distribution		
data sample size	4359 people	4590 people

(data from NHANES 2006 study, weighted for USA demographics)

Distribución del índice de masa corporal

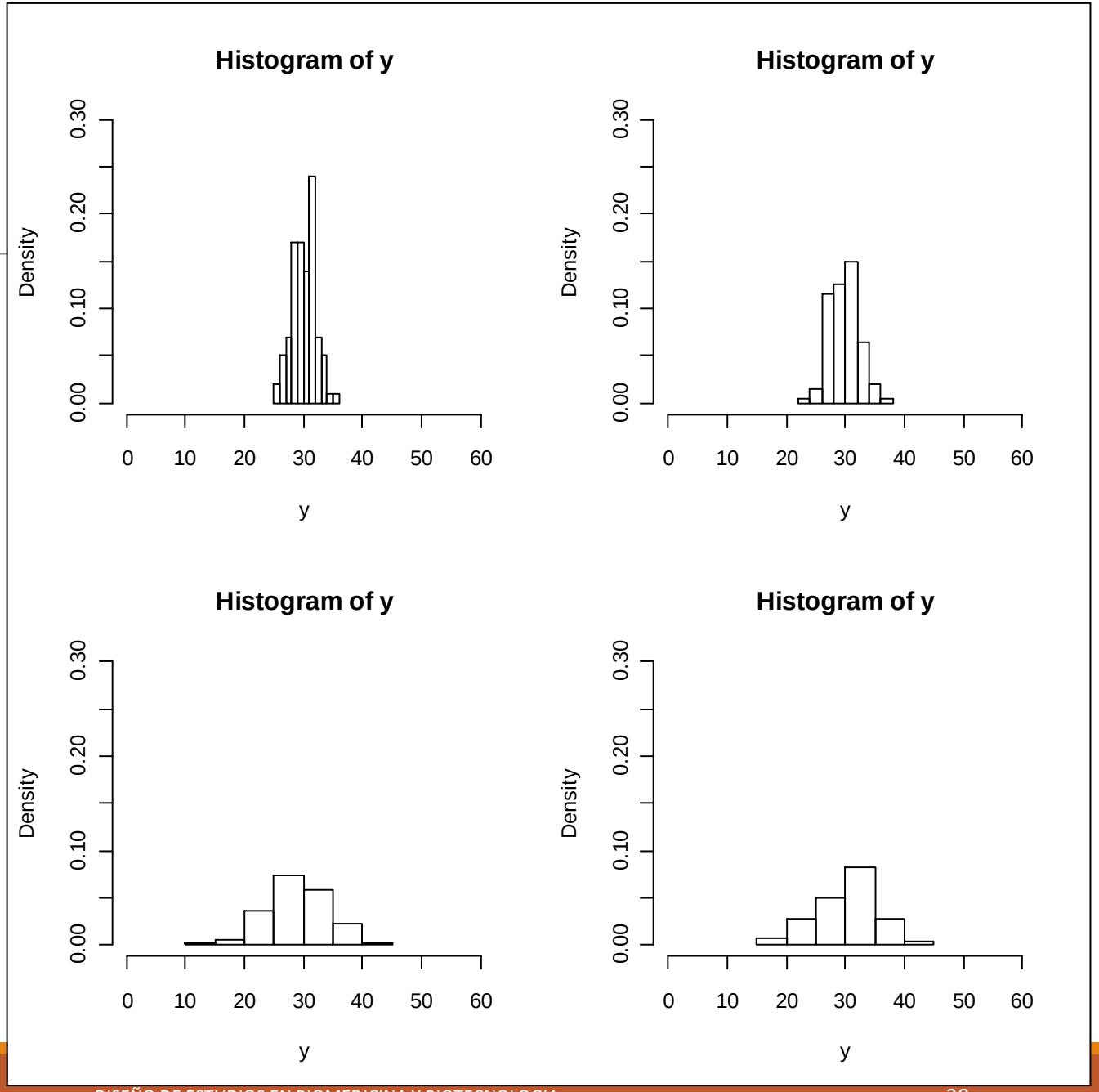
	male, (25 to 35) years	female, (25 to 35) years
95% reference range	(19.9 to 47)	(18.8 to 45)
$\pm 1\sigma$ range	(21.8 to 35)	(20.8 to 35)
distribution		
data sample size	424 people	594 people

(data from NHANES 2006 study, weighted for USA demographics)

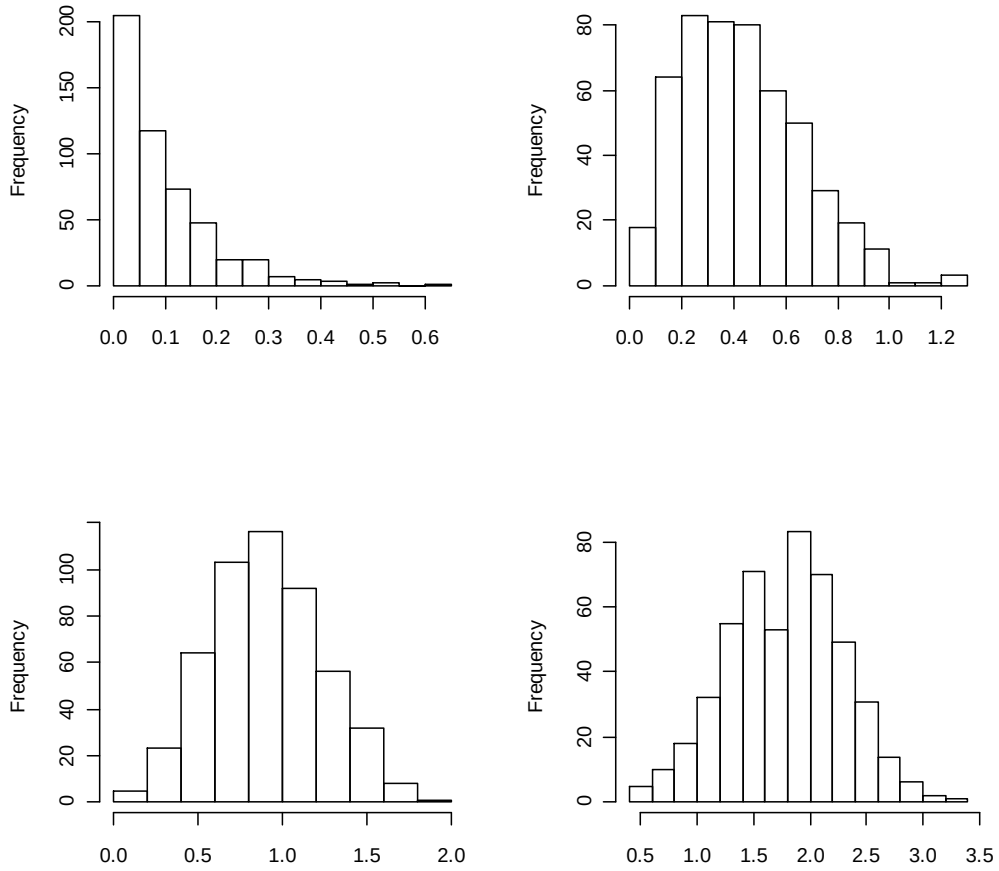
	male, (55 to 65) years	female, (55 to 65) years
95% reference range	(20.7 to 43)	(18.7 to 49)
$\pm 1\sigma$ range	(23.9 to 35)	(22.1 to 38)
distribution		
data sample size	335 people	338 people

(data from NHANES 2006 study, weighted for USA demographics)

Valor medio y dispersión



Asimetría en la variabilidad



Modelo estadístico básico

Se espera un valor medio μ en cada observación.

La distribución de ε_i explica la dispersión alrededor de la media

$$y_i = \mu + \varepsilon_i$$

$$\varepsilon_i \rightarrow \text{Distribución}$$

Modelo lineal

El género tiene un efecto sobre el nivel de colesterol

$$y_{ij} = \mu + \alpha_i + \varepsilon_{ij}$$

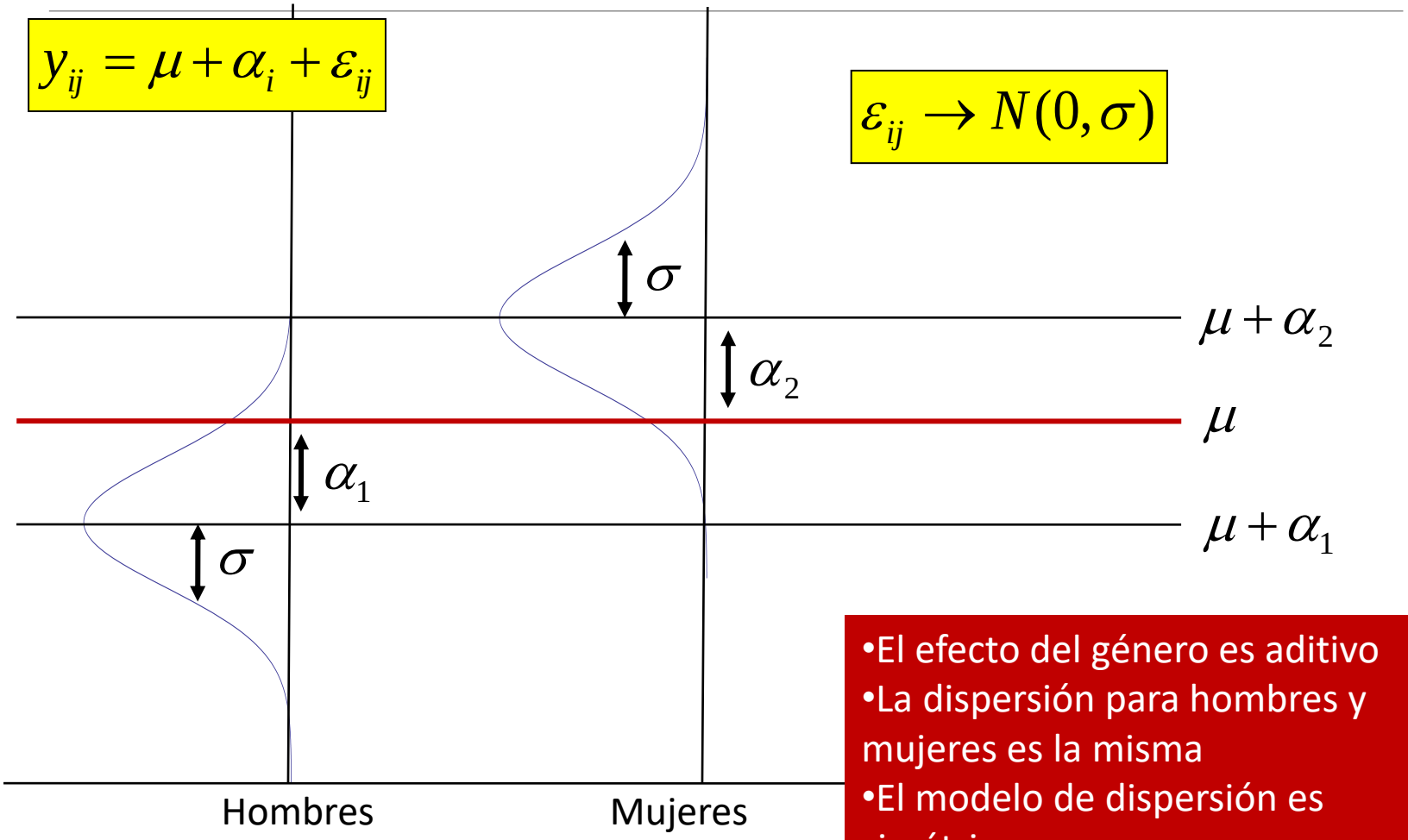
$y_{ij} \rightarrow$ Colesterol en el individuo j del grupo i

$\mu \rightarrow$ Media general

$\alpha_i \rightarrow$ Efecto del grupo i

$\varepsilon_{ij} \rightarrow$ Variabilidad en el individuo j del grupo i

Efecto del género en el valor de una variable



- El efecto del género es aditivo
- La dispersión para hombres y mujeres es la misma
- El modelo de dispersión es simétrico

Modelo lineal

El nivel de colesterol varia con la edad y el género

$$y_{ij} = \mu + \alpha_i + \beta_i \; X + \varepsilon_{ij}$$

$y_{ij} \rightarrow$ Colesterol en el individuo j del grupo i con edad X

$\mu \rightarrow$ Media general

$\alpha_i \rightarrow$ Efecto del grupo i

$\beta_i \rightarrow$ Efecto de la edad en el grupo i

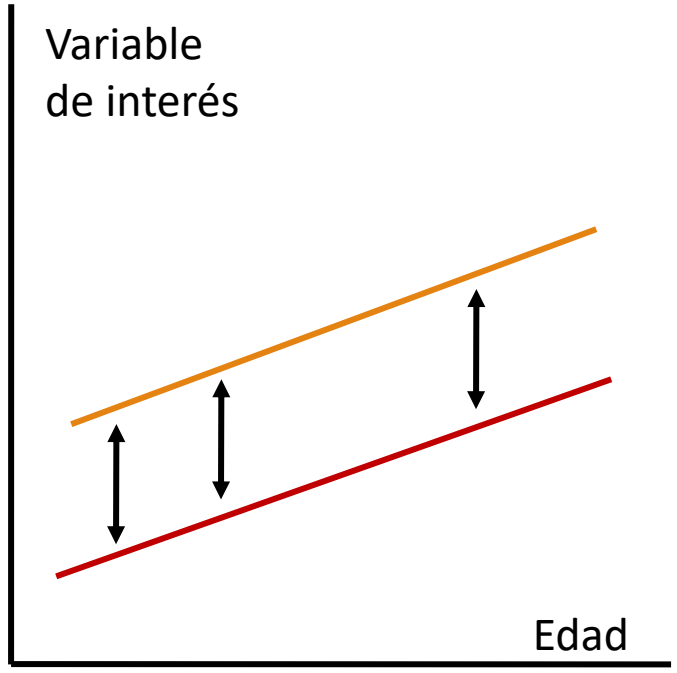
$X \rightarrow$ Edad

$\varepsilon_{ij} \rightarrow$ Variabilidad en el individuo j del grupo i con edad X

Variación en función del género y la edad

$$y_{ij} = \mu + \alpha_i + \beta_i \; X + \varepsilon_{ij}$$

$$\alpha_1 \neq \alpha_2 \qquad \beta_1 = \beta_2$$



En este caso, la variable de interés varia de forma lineal con la edad. Hombres y mujeres difieren de forma constante para cada edad

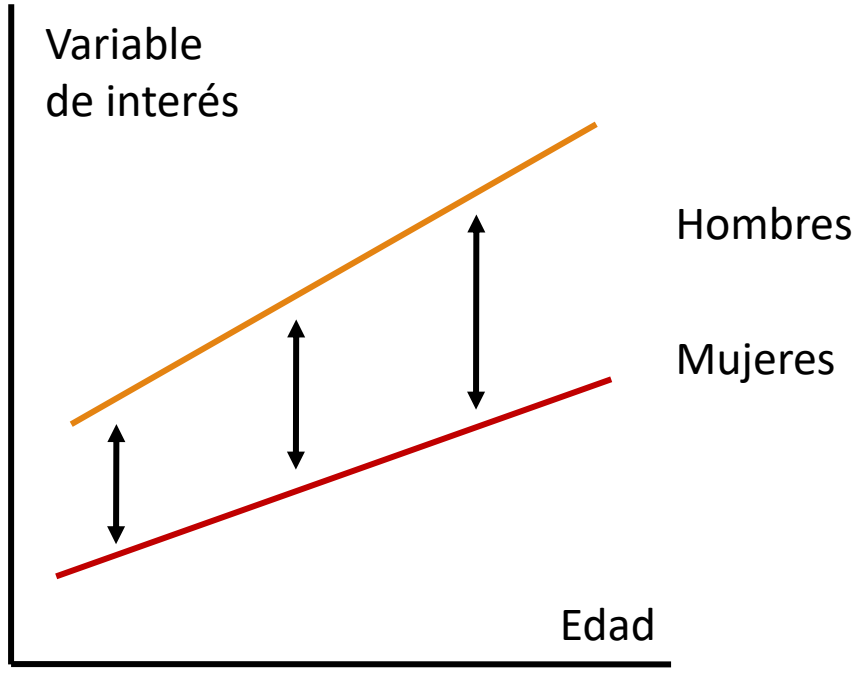
Efecto del género

Para cada edad, los hombres y mujeres presentan valores de la variable de interés con una dispersión similar.

Variación en función del género y la edad (interacción)

$$y_{ij} = \mu + \alpha_i + \beta_i X + \varepsilon_{ij}$$

$$\alpha_1 \neq \alpha_2 \qquad \beta_1 \neq \beta_2$$



En este caso, la variable de interés varia de forma lineal con la edad. El efecto es mayor para hombres. Para una edad determinada, el efecto del género es distinto.

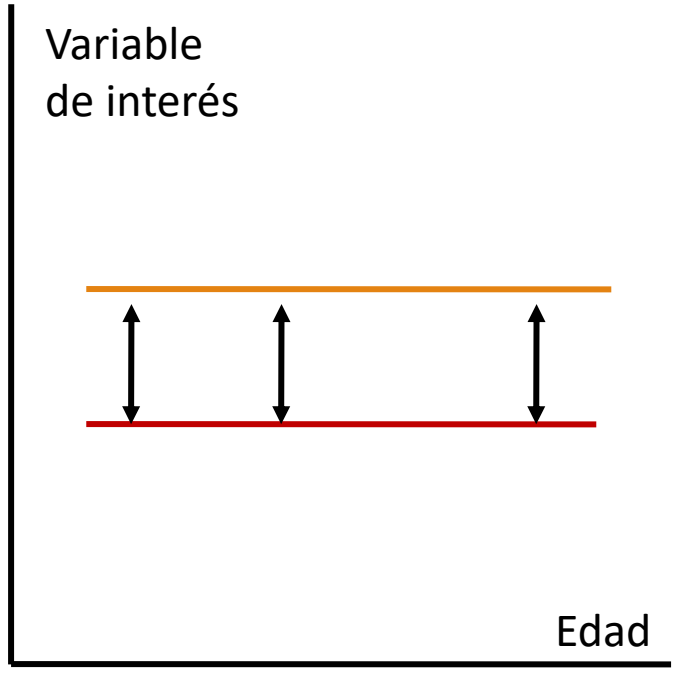
Efecto del género

Para cada edad, los hombres y mujeres presentan valores de la variable de interés con una dispersión similar.

Variación en función del género y la edad (independencia)

$$y_{ij} = \mu + \alpha_i + \beta_i X + \varepsilon_{ij}$$

$$\alpha_1 \neq \alpha_2 \qquad \beta_1 = \beta_2 = 0$$



En este caso, la variable de interés es independiente de la edad. El efecto del género es constante para cada edad. Los hombres tienen un valor medio superior a las mujeres.

Efecto del género

Para cada edad, los hombres y mujeres presentan valores de la variable de interés con una dispersión similar.

Cuestiones básicas a considerar cuando se diseña un estudio

Definir claramente los objetivos del estudio

Definir la población objeto de estudio

Evaluar qué tipo de estudio es más conveniente en función de los objetivos y de la población objeto

Determinar qué tamaño muestral es el más adecuado en función del objetivo que se persigue

Establecer un protocolo de recogida de datos (en el caso de estudios observacionales) o de experimentación (en caso de estudios experimentales)

Determinar de antemano qué análisis estadístico se va a aplicar una vez se disponga de los datos