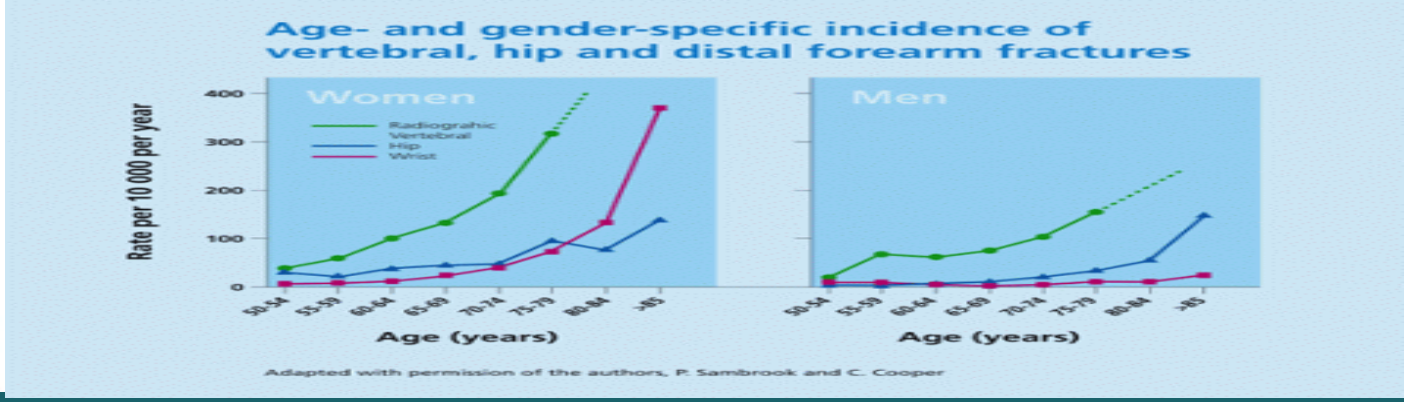



# De las epidemias de cólera a la crisis de los pepinos

## El desarrollo de la bioestadística y la epidemiología

Universidad de Cantabria

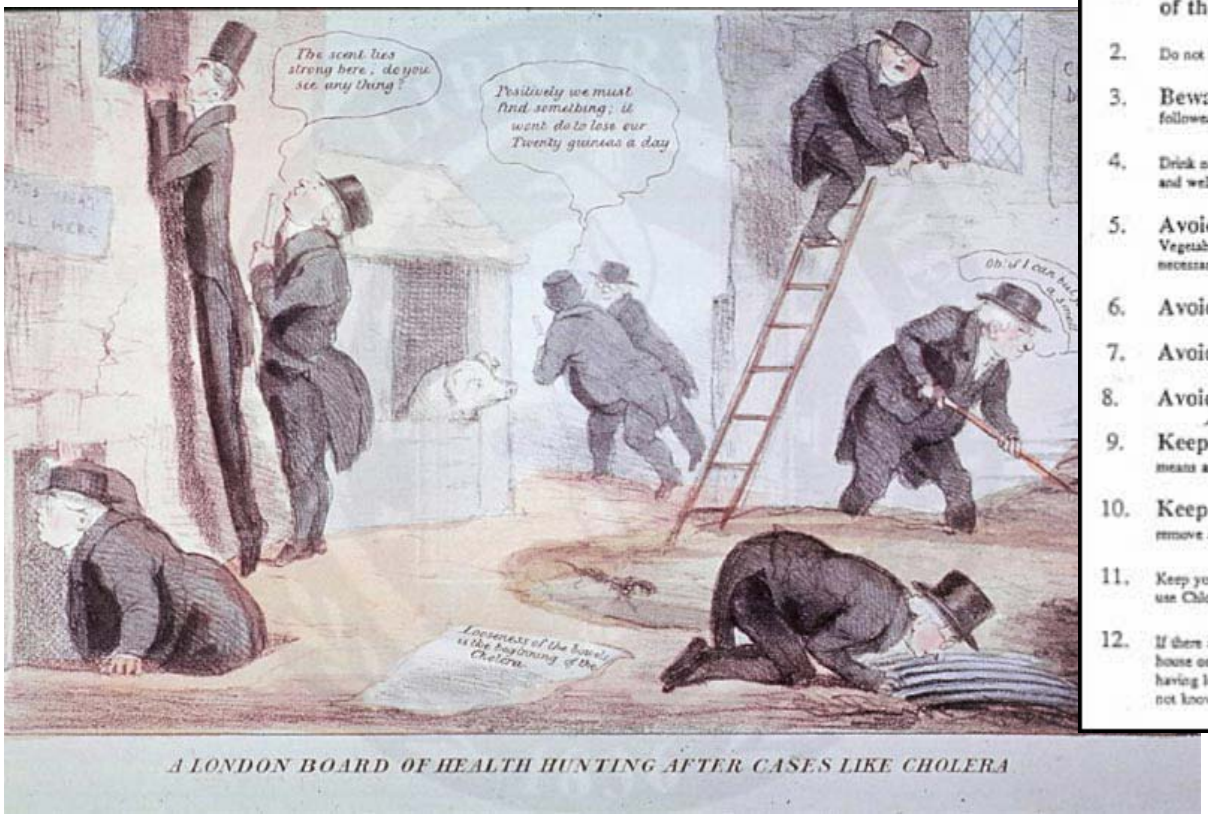
Javier Llorca
Epidemiología


Estadística básica
Bioestadística
Epidemiología general
Epidemiología clínica
Clínica médica

# Índice


- De las epidemias de cólera...
  - Fases en el desarrollo de la epidemiología
  - Tipos de estudio
  - Herramientas de cálculo en la epidemiología actual
  - ¿Para qué sirve la epidemiología?
  - Nuestros problemas actuales
  - ... hasta la crisis de los pepinos

# De las epidemias de cólera...




A LONDON BOARD OF HEALTH HUNTING AFTER CASES LIKE CHOLERA

## GENERAL BOARD of HEALTH.

PRECAUTIONS
AGAINST

## CHOLERA.

1. Apply for Medicine immediately to stop Looseness of the Bowels, or it may bring on Cholera.
2. Do not take any strong opening Medicine without Medical advice
3. Beware of Drink, for excess in Beer, Wine, or Spirit is likely to be followed by Cholera.
4. Drink no Water which has not been boiled; and avoid that which is not quite clear and well tasted.
5. Avoid eating Meat that is tainted, decayed or unripe Fruit, and stale Fish or raw Vegetables. Cooked Vegetables, or ripe and cooked Fruit, in moderation, are a necessary part of diet at all times.
6. Avoid fasting to long; be moderate at meals.
7. Avoid great fatigue, and getting heated and then chilled.
8. Avoid getting wet, or remaining in wet clothes.
9. Keep yourself clean, and your body and feet as dry and as warm as your means and occupation will permit.
10. Keep your rooms well cleaned and lime-washed; remove all dirt and impurities immediately.
11. Keep your windows open as much as possible to admit fresh air; and, if necessary, use Chloride of Lime or Zinc to remove any offensive smells.
12. If there are any dust or dirt heaps, foul drains, bad smells, or other nuisances in the house or neighbourhood, make complaint without delay to the Local Authorities having legal powers to remove them, or if there be no such authorities, or if you do not know who they are, complain to the Board of Guardians.

Javier Llorca.
Epidemiología

# De las epidemias de cólera...

*"We know nothing; we are at sea in a whirlpool of ignorance"*
*Lancet, 22 October 1853:393-4 (editorial)*

# De las epidemias de cólera...

- William Farr (1807 – 1883)
  - *Compiler of Statistics in the General Register Office*
  - Estadísticas vitales periódicamente
  - Concepto de personas-tiempo
  - Concepto de ajuste de tasas

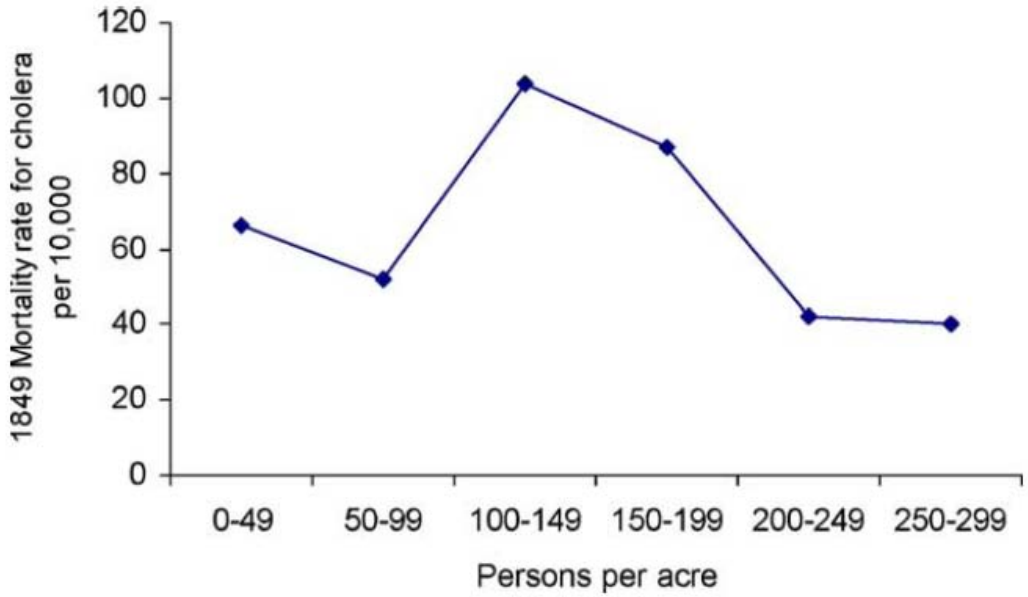
# De las epidemias de cólera...

*"By studying the causes which are injurious and fatal to men in our countries and in our cities, statists will contribute to the removal of evils which shorten human life and to the improvement of the race of men*

*William Farr*

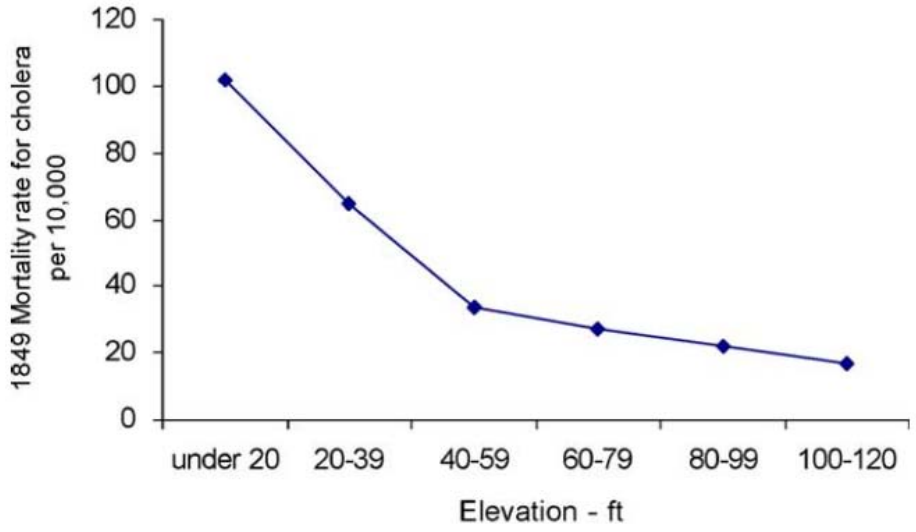
# De las epidemias de cólera...

- William Farr (1807 – 1883)



# De las epidemias de cólera...

- William Farr (1807 – 1883)



# De las epidemias de cólera...

- John Snow (1813 – 1858)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# De las epidemias de có

- John Snow (1813 – 1

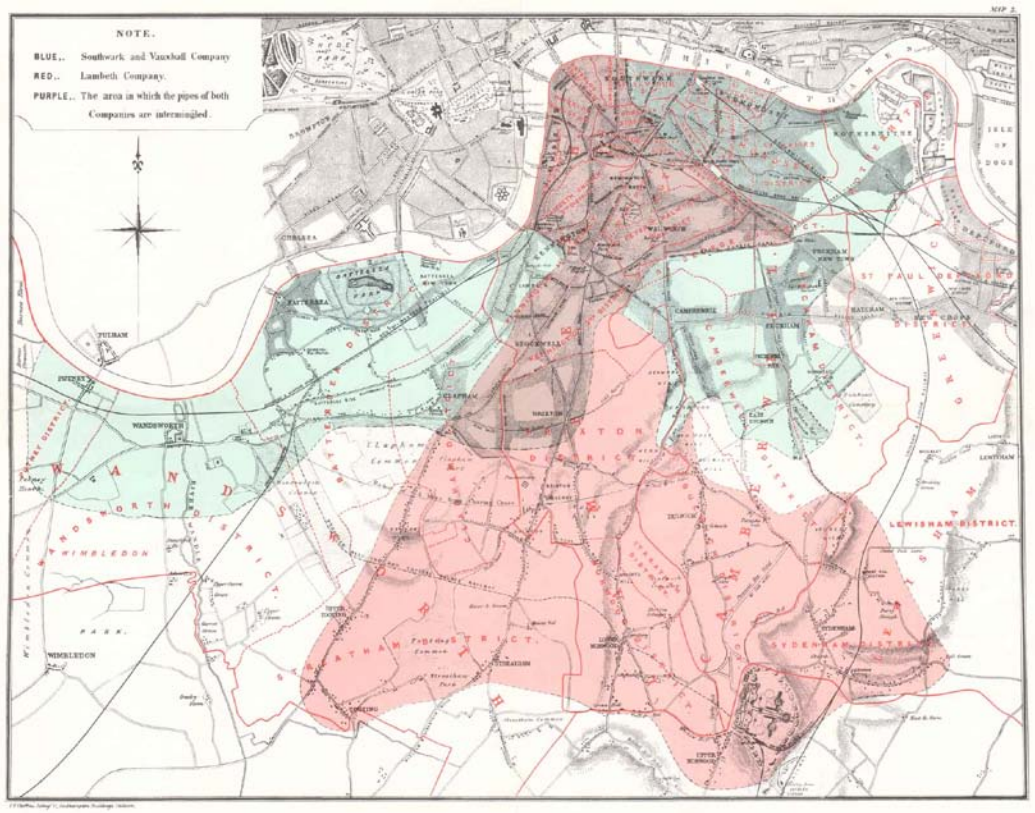
# De las epidemias de cólera...

- John Snow (1813 – 1858)
  - Epidemia de cólera en Londres, 1854

| Company | Number of houses | Deaths from cholera | Deaths / 10000 houses |
|---|---|---|---|
| Southwark and Vauxhall | 40046 | 1263 | 315 |
| Lambeth | 26107 | 98 | 37 |
| Rest of London | 256423 | 1422 | 59 |

# De las epidemias de cólera...

- John Snow (1813 – 1858)
  - Epidemia de cólera en Londres, 1854



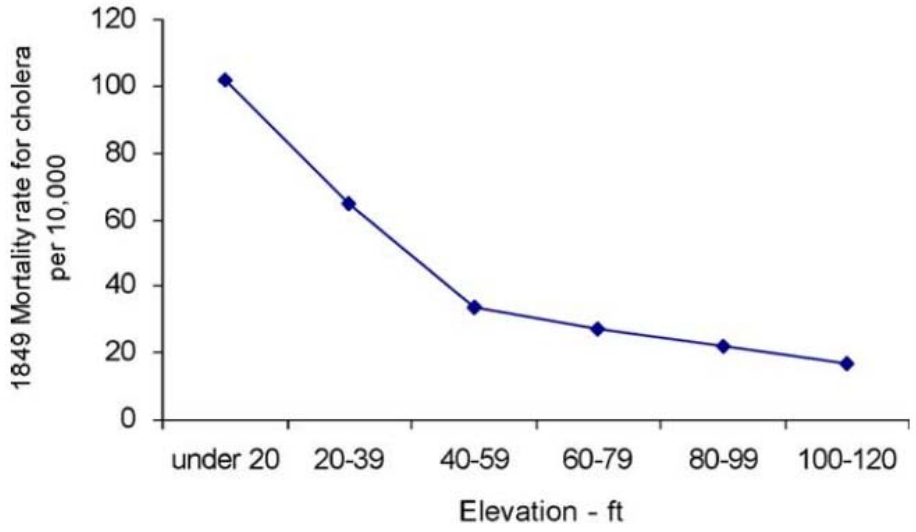
# De las epidemias de cólera...

- John Snow (1813 – 1858)


George Cruickshank's depiction of the portion of the River Thames from which the Southwark Water Works drew its supply, circa 1830.

# De las epidemias de cólera...

- William Farr (1807 – 1883)



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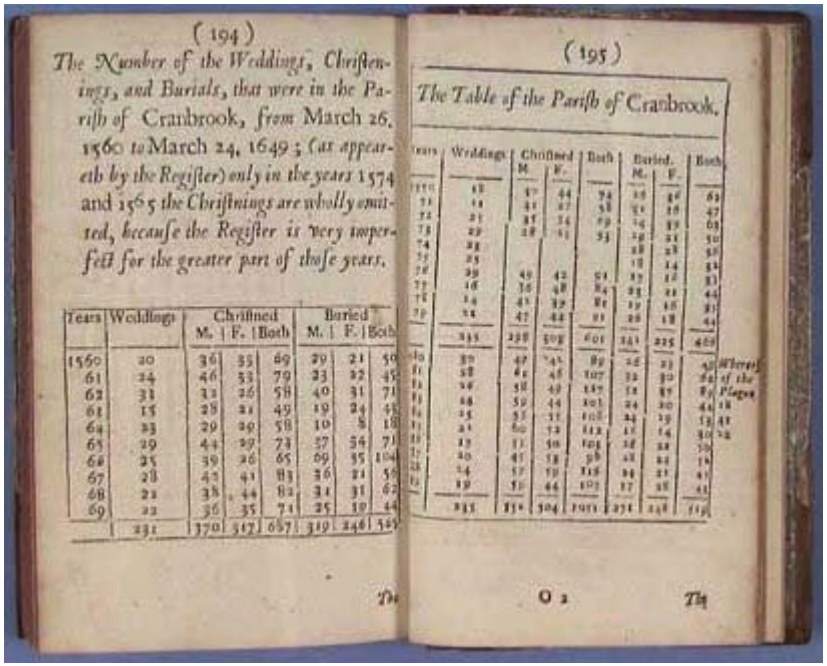
# Historia de la epidemiología

| Años | Era | Paradigma | Medidas preventivas |
|---|---|---|---|
| hasta 1850 | Estadísticas sanitarias | Miasmas | Drenaje, saneamiento |
| 1850 – 1950 | Enfermedades infecciosas | Teoría de gérmenes | Vacunas, aislamiento, cuarentena |
| 1950 - | Enfermedades crónicas | Caja negra | Modificar el estilo de vida, el agente o el ambiente |

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- John Graunt (1620 – 1674)
  - *Natural and Political Observations made upon the Bills of Mortality* (1662)



(194)

*The Number of the Weddings, Christenings, and Burials, that were in the Parish of* Cranbrook, *from* March 26. 1560 *to* March 24. 1649 ; *(as appeareth by the Register) only in the years* 1574 *and* 1565 *the Christnings are wholly omitted, because the Register is very imperfect for the greater part of those years.*

| Years | Weddings | Christned M. | Christned F. | Christned Both | Buried M. | Buried F. | Buried Both |
|---|---|---|---|---|---|---|---|
| 1560 | 20 | 36 | 33 | 69 | 29 | 21 | 50 |
| 61 | 24 | 46 | 33 | 79 | 23 | 22 | 45 |
| 62 | 31 | 33 | 26 | 58 | 40 | 31 | 71 |
| 63 | 15 | 25 | 21 | 49 | 19 | 24 | 43 |
| 64 | 33 | 29 | 29 | 58 | 10 | 8 | 18 |
| 65 | 29 | 44 | 29 | 73 | 57 | 54 | 71 |
| 66 | 25 | 39 | 26 | 65 | 69 | 35 | 104 |
| 67 | 28 | 45 | 41 | 83 | 36 | 21 | 57 |
| 68 | 21 | 38 | 44 | 82 | 31 | 31 | 62 |
| 69 | 22 | 36 | 35 | 71 | 25 | 19 | 44 |
| | 231 | 370 | 317 | 687 | 319 | 246 | 565 |

(195)

*The Table of the Parish of* Cranbrook.

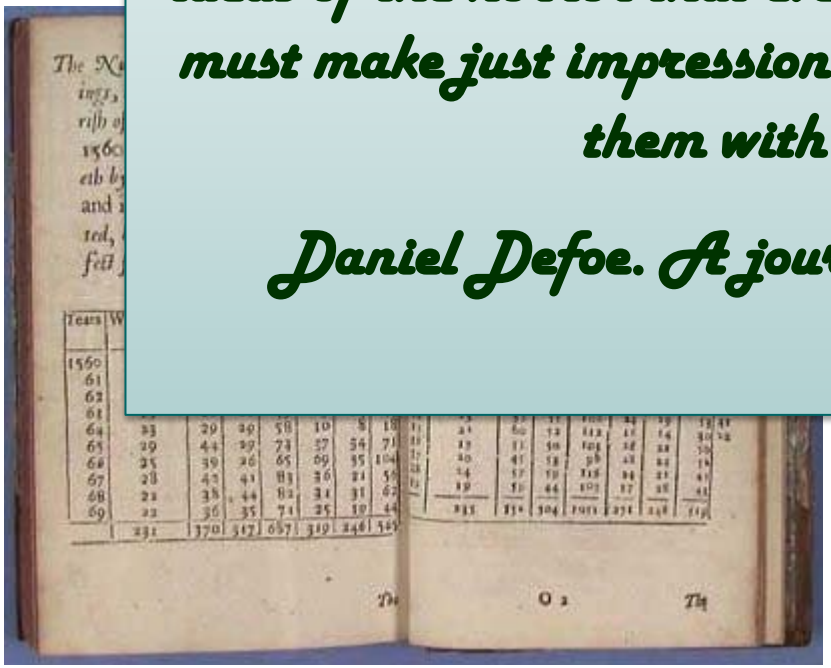
| Years | Weddings | Christned M. | Christned F. | Christned Both | Buried M. | Buried F. | Buried Both | |
|---|---|---|---|---|---|---|---|---|
| 70 | 22 | 47 | 42 | 89 | 22 | 23 | 45 | Where of the Plague |
| 71 | 28 | 48 | 48 | 107 | 32 | 30 | 62 | |
| 72 | 36 | 58 | 49 | 107 | 18 | 27 | 45 | |
| 73 | 48 | 59 | 44 | 103 | 24 | 20 | 44 | |
| 74 | 25 | 53 | 51 | 104 | 24 | 19 | 43 | |
| 75 | 21 | 60 | 52 | 112 | 22 | 14 | 36 | |
| 76 | 23 | 53 | 50 | 103 | 28 | 28 | 56 | |
| 77 | 20 | 41 | 58 | 99 | 28 | 22 | 50 | |
| 78 | 14 | 57 | 58 | 115 | 24 | 21 | 45 | |
| 79 | 19 | 51 | 44 | 95 | 17 | 25 | 42 | |
| | 255 | 470 | 434 | 904 | 251 | 238 | 489 | |

O 2

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

*"Were it possible to represent those times exactly to those that did not see them, and give the reader due ideas of the horror that everywhere presented itself, it must make just impressions upon their minds and fill them with surprise."*

*Daniel Defoe. A journal of the plague year*

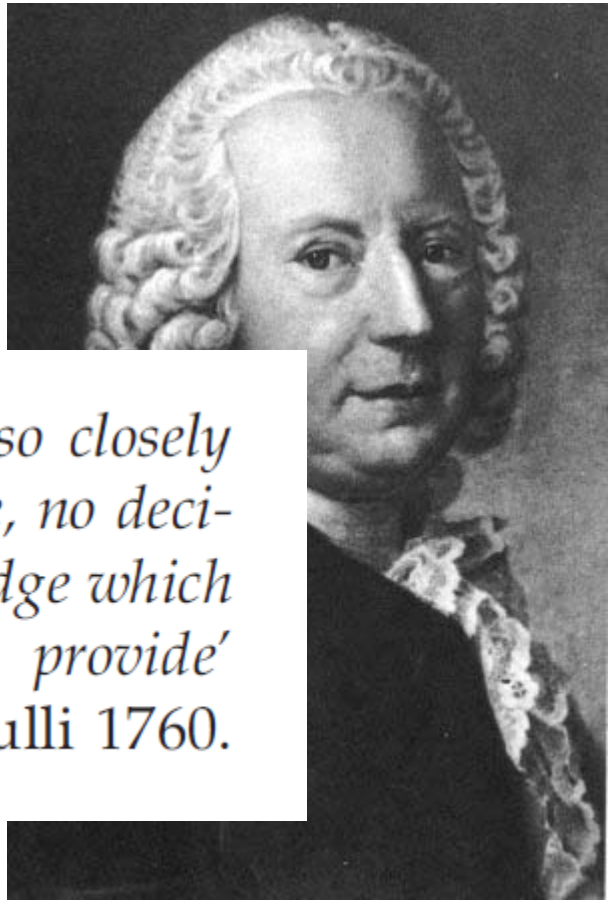


# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- James Lind (1716 – 1794)
  - Médico de la Armada (*HMS Salisbury*)
  - Tratamiento del escorbuto
    - Un cuarto de sidra
    - 25 gotas de elixir de vitriolo
    - 6 cucharadas de vinagre
    - Media pinta de agua de mar
    - 2 naranjas y 1 limón
    - Pasta con especias + agua de cebada

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- Daniel Bernoulli (1700-1782)



*'I simply wish that, in a matter which so closely concerns the wellbeing of the human race, no decision shall be made without all the knowledge which a little analysis and calculation can provide'*

Daniel Bernoulli 1760.

Table 1

| Age in years | Survivors according to M. Halley | Not having had smallpox | Having had smallpox | Catching smallpox each year | Dying of smallpox each year | Total smallpox deaths | Deaths from other diseases each year |
|---|---|---|---|---|---|---|---|
| 0 | 1,300 | 1,300 | 0 | | | | |
| 1 | 1,000 | 896 | 104 | 137 | 17.1 | 17.1 | 283 |
| 2 | 855 | 685 | 170 | 99 | 12.4 | 29.5 | 133 |
| 3 | 798 | 571 | 227 | 78 | 9.7 | 39.2 | 47 |
| 4 | 760 | 485 | 275 | 66 | 8.3 | 47.5 | 30 |
| 5 | 732 | 416 | 316 | 56 | 7.0 | 54.5 | 21 |
| 6 | 710 | 359 | 351 | 48 | 6.0 | 60.5 | 16 |
| 7 | 692 | 311 | 381 | 42 | 5.2 | 65.7 | 12.8 |
| 8 | 680 | 272 | 408 | 36 | 4.5 | 70.2 | 7.5 |
| 9 | 670 | 237 | 433 | 32 | 4.0 | 74.2 | 6 |
| 10 | 661 | 208 | 453 | 28 | 3.5 | 77.7 | 5.5 |
| 11 | 653 | 182 | 471 | 24.4 | 3.0 | 80.7 | 5 |
| 12 | 646 | 160 | 486 | 21.4 | 2.7 | 83.4 | 4.3 |
| 13 | 640 | 140 | 500 | 18.7 | 2.3 | 85.7 | 3.7 |
| 14 | 634 | 123 | 511 | 16.6 | 2.1 | 87.8 | 3.9 |
| 15 | 628 | 108 | 520 | 14.4 | 1.8 | 89.6 | 4.2 |
| 16 | 622 | 94 | 528 | 12.6 | 1.6 | 91.2 | 4.4 |
| 17 | 616 | 83 | 533 | 11.0 | 1.4 | 92.6 | 4.6 |
| 18 | 610 | 72 | 538 | 9.7 | 1.2 | 93.8 | 4.8 |
| 19 | 604 | 63 | 541 | 8.4 | 1.0 | 94.8 | 5 |
| 20 | 598 | 56 | 542 | 7.4 | 0.9 | 95.7 | 5.1 |
| 21 | 592 | 48.5 | 543 | 6.5 | 0.8 | 96.5 | 5.2 |
| 22 | 586 | 42.5 | 543 | 5.6 | 0.7 | 97.2 | 5.3 |
| 23 | 579 | 37 | 542 | 5.0 | 0.6 | 97.8 | 6.4 |
| 24 | 572 | 32.4 | 540 | 4.4 | 0.5 | 98.3 | 6.5 |

Table 2

| Ages by years | Natural state with smallpox | State without smallpox | Difference or gain |
|---|---|---|---|
| 0 | 1,300 | 1.300 | 0 |
| 1 | 1,000 | 1,017.1 | 17.1 |
| 2 | 855 | 881.8 | 26.8 |
| 3 | 798 | 833.3 | 35.3 |
| 4 | 760 | 802.0 | 42.0 |
| 5 | 732 | 779.8 | 47.8 |
| 6 | 710 | 762.8 | 52.8 |
| 7 | 692 | 749.1 | 57.2 |
| 8 | 680 | 740.9 | 60.9 |
| 9 | 670 | 734.4 | 64.4 |
| 10 | 661 | 728.4 | 67.4 |
| 11 | 653 | 722.9 | 69.9 |
| 12 | 646 | 718.2 | 72.2 |
| 13 | 640 | 741.1* | 74.1 |
| 14 | 634 | 709.7 | 75.7 |
| 15 | 628 | 705.0 | 77.0 |
| 16 | 622 | 700.1 | 78.1 |
| 17 | 616 | 695.0 | 79.0 |
| 18 | 610 | 689.6 | 79.6 |
| 19 | 604 | 684.0 | 80.0 |
| 20 | 598 | 678.2 | 80.2 |
| 21 | 592 | 672.3 | 80.3 |
| 22 | 586 | 666.3 | 80.3 |
| 23 | 579 | 659.0 | 80.0 |
| 24 | 572 | 651.7 | 79.7 |
| 25 | 565 | 644.3 | 79.3 |

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- Edwin Chadwick (1800 – 1890)

- Hasta 1840:
  - Pobreza → Enfermedad → Inestabilidad política
  - Promueve la Ley de Pobreza (1832)

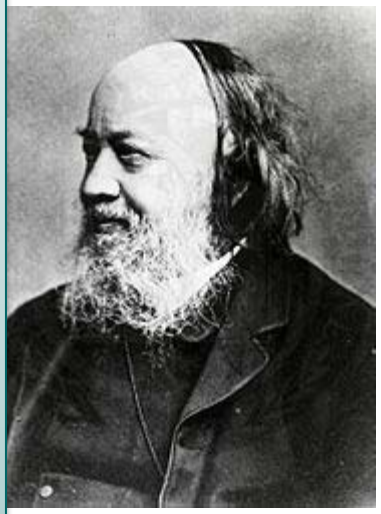
# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- Edwin Chadwick (1800 – 1890)

- Desde 1840:
  - Enfermedad → Pobreza → Inestabilidad política
  - Publica *An Inquiry into the Sanitary Condition of the Labouring Population of Great Britain of 1842*
  - Promueve alcantarillado y recogida de basuras

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

*"That such disease, wherever its attacks are frequent, is always found in connection with the physical circumstances above specified, and that where those circumstances are removed by drainage, proper cleansing, better ventilation, and other means of diminishing atmospheric impurity, the frequency and intensity of such disease is abated; and where the removal of the noxious agencies appears to be complete, such disease almost entirely disappears.*
*Edwin Chadwick*



# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- El Comité de Pobreza de la Asamblea Nacional propone la contratación de médicos por barrios
- El Comité de Salud de la Asamblea Nacional lo rechaza
  - Guillotin (1738 – 1814)

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- Pièrre Alexander Louis (1787-1872)

Resultados del sangrado con sanguijuelas para tratar neumonías (1835)

| Sangrado: Días tras el inicio de la neumonía | Muertos | Supervivientes |
|---|---|---|
| 1-3 | 12 | 12 |
| 4-6 | 12 | 22 |
| 7-9 | 3 | 16 |

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

*"I conceive that without the aid of statistics nothing like real medical science is possible"*

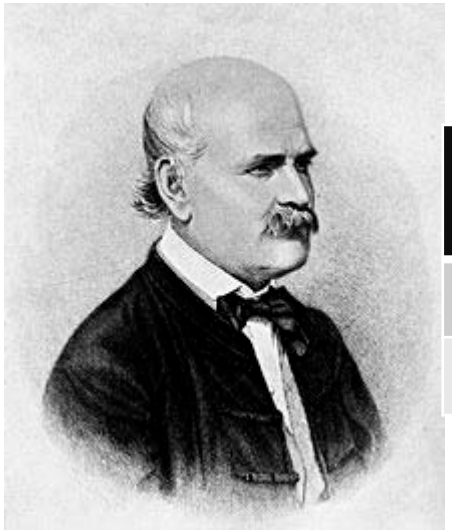
*Pièrre Charles Alexander Louis*

# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- Se empiezan a utilizar herramientas estadísticas en salud pública
- Se toman medidas de saneamiento basándose en la teoría de los miasmas
- La teoría era falsa pero…
- Las medidas fueron muy eficaces

# Historia de la epidemiología: Enfermedades infecciosas

- Ignacio Semmelweis (1818 – 1865)



**Mortalidad en dos clínicas, 1833-1840**

| ¿Se hacían autopsias? | Partos | Muertes | % |
|---|---|---|---|
| No | 71395 | 897 | 1.25 |
| Sí | 28429 | 1509 | 5.30 |

# Historia de la epidemiología: Enfermedades infecciosas

- Ignacio Semmelweis (1818 – 1865)

**Mortalidad en dos clínicas, 1847-1858**

| | Partos | Muertes | % |
|---|---|---|---|
| Clínica 1 (estudiantes de medicina) | 20042 | 1989 | 6.56 |
| Clínica 2 (estudiantes de matrona) | 17791 | 691 | 3.38 |

# Historia de la epidemiología: Enfermedades infecciosas

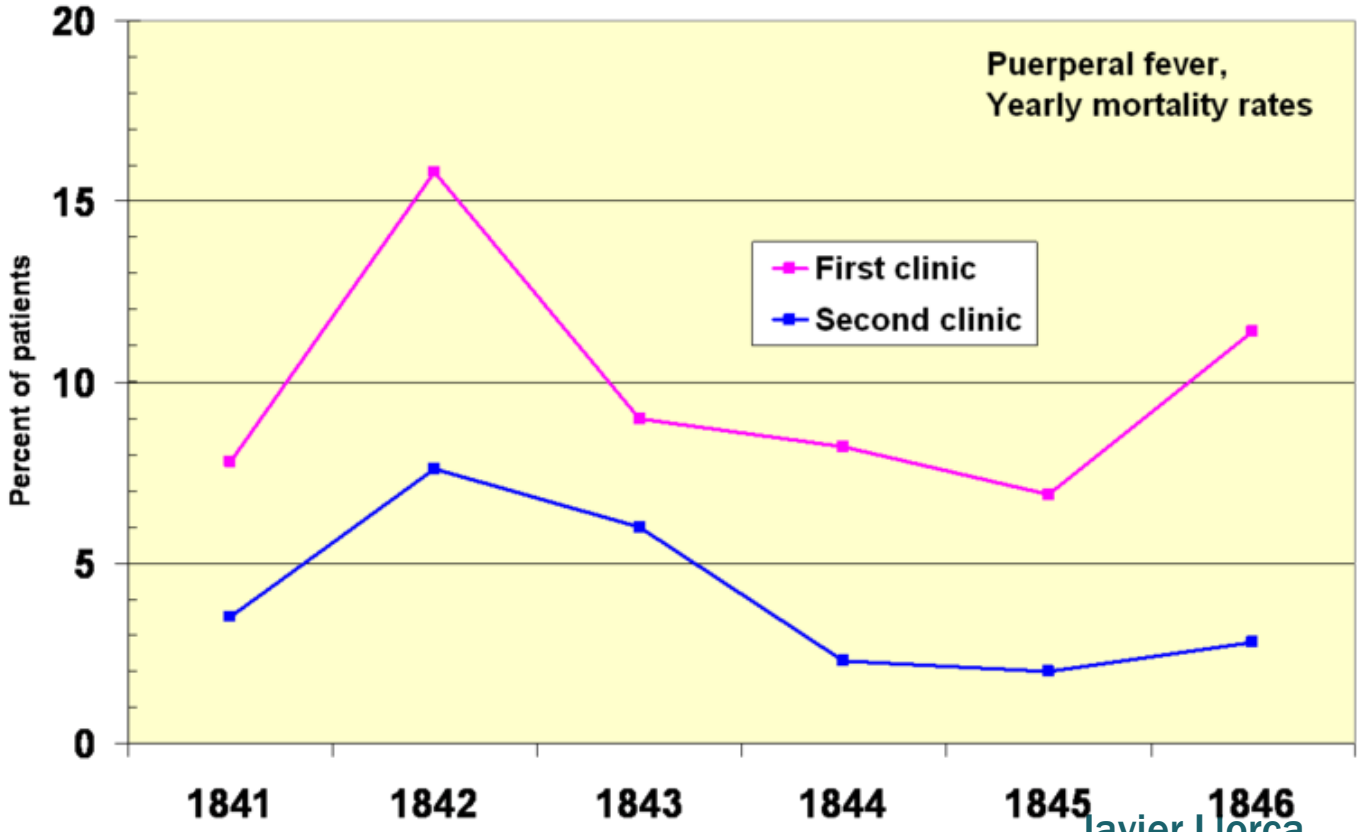
- Ignacio Semmelweis (1818 – 1865)

**Mortalidad en dos clínicas, 1847-1858**
**Después de introducir el lavado de manos con solución de lejía**

| | Partos | Muertes | % |
|---|---|---|---|
| Clínica 1 (estudiantes de medicina) | 47938 | 1712 | 3.57 |
| Clínica 2 (estudiantes de matrona) | 40770 | 1248 | 3.06 |

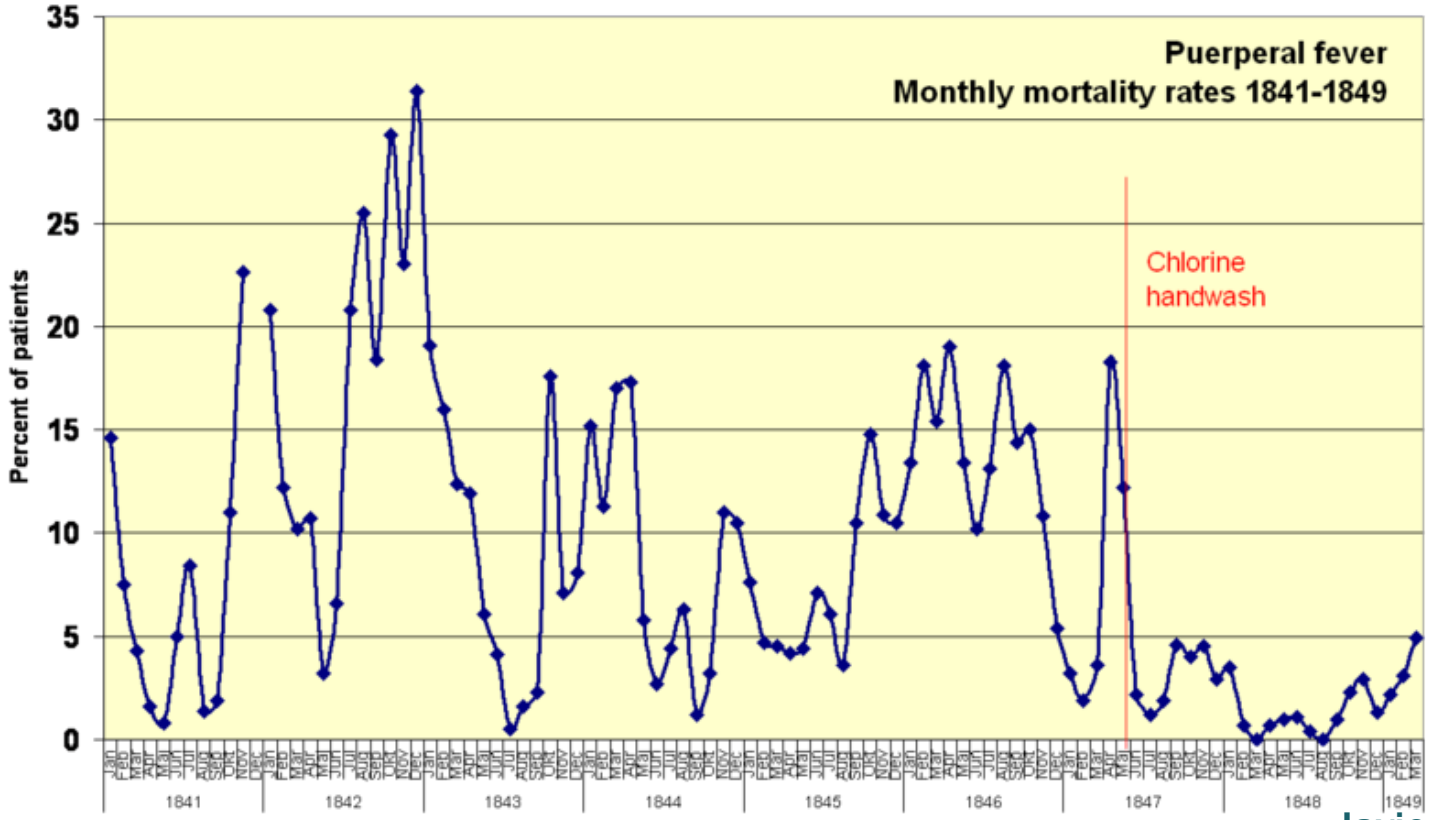
# Historia de la epidemiología: Enfermedades infecciosas

- Ignacio Semmelweis (1818 – 1865)



# Historia de la epidemiología: Enfermedades infecciosas

- Ignacio Semmelweis (1818 – 1865)



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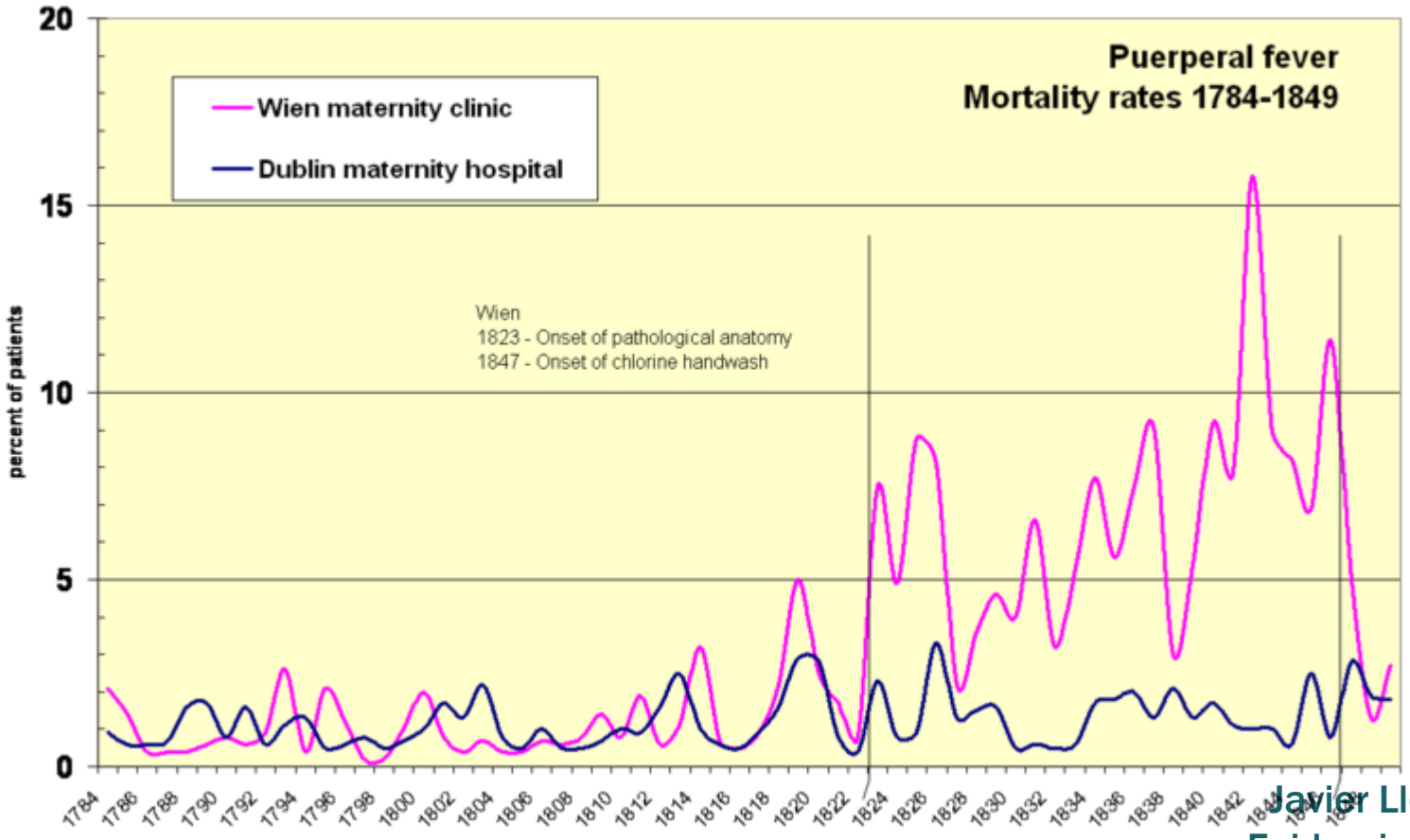
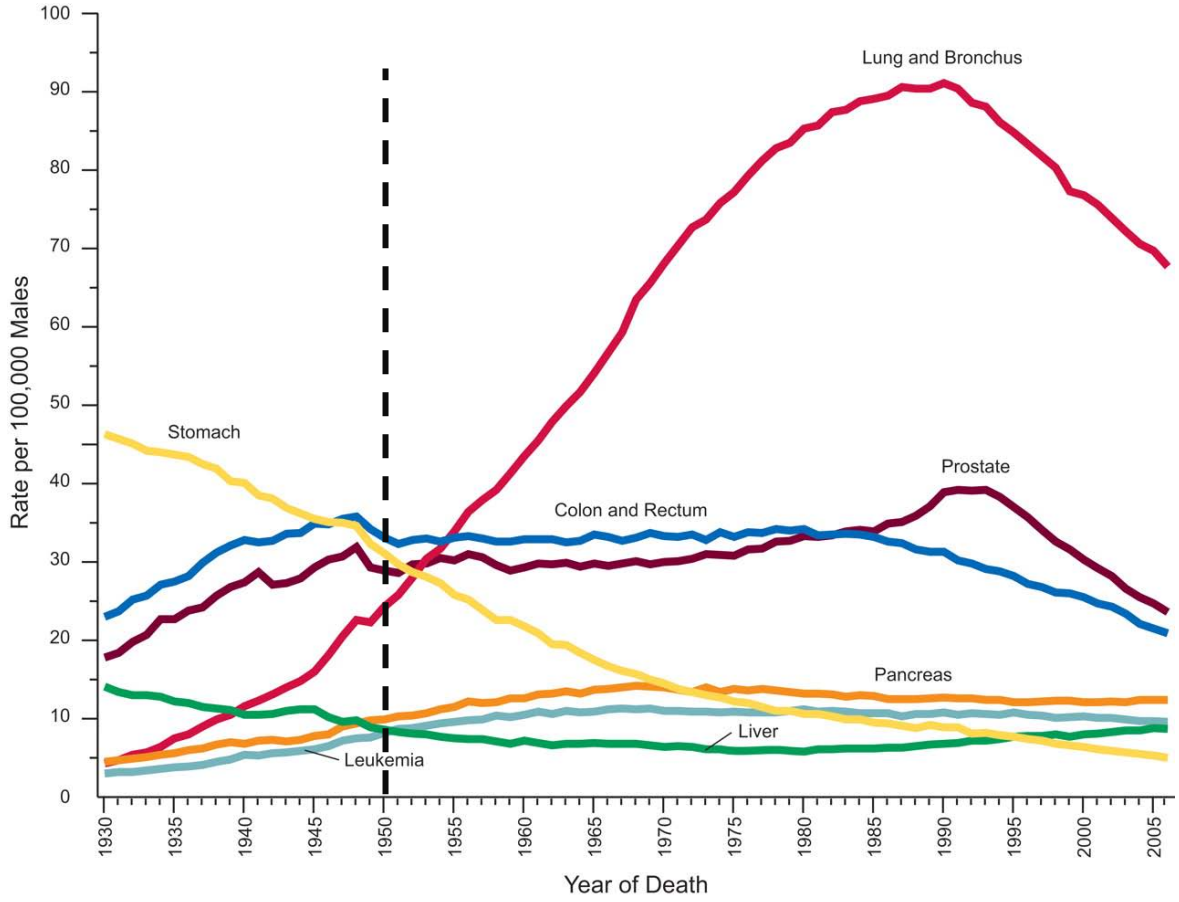
- Ignacio Semmelweis (1818 – 1865)



# Historia de la epidemiología: Enfermedades infecciosas

- Búsqueda del agente por medios de laboratorio
- UNICAUSALIDAD
- DESAPARECE EL GRUPO DE COMPARACIÓN
- Estudios a corto plazo
- Medidas de prevención:
  - Vacunas
  - Aislamiento
  - Cuarentena
  - Antibióticos (más tarde)

# Historia de la epidemiología: Enfermedades crónicas




**From Jemal, A. et al.**
**CA Cancer J Clin 2010;0:caac.20073v1**

# Historia de la epidemiología: Enfermedades crónicas

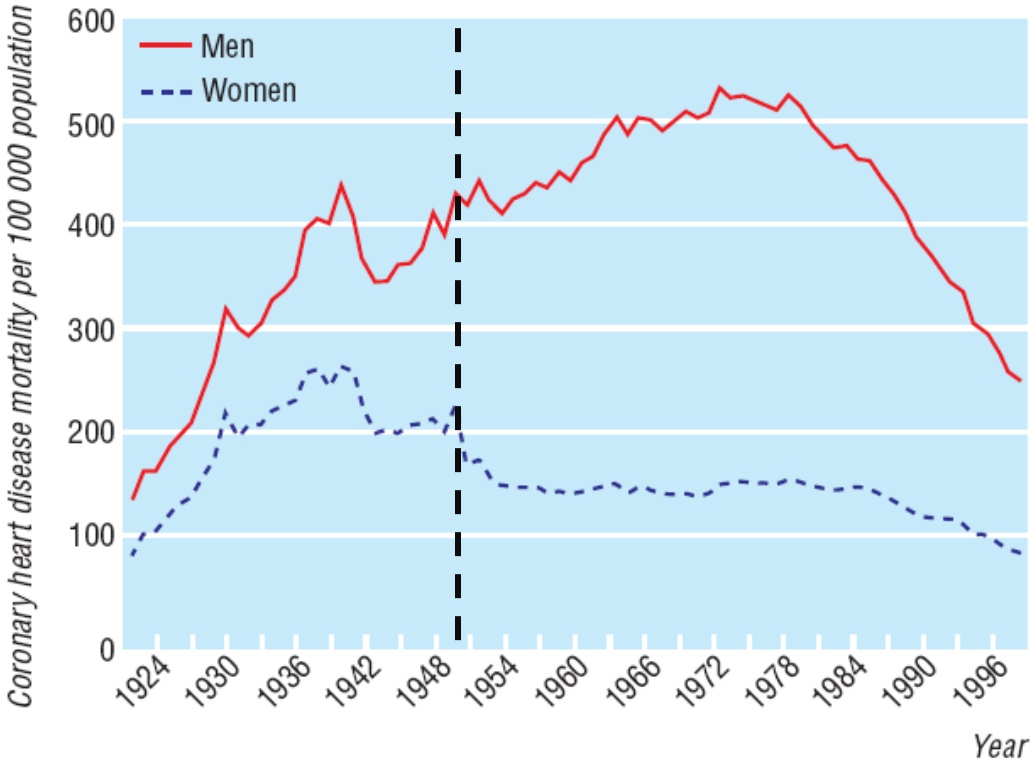



**Fig 1** Secular trends in age standardised mortality per 100 000 population from coronary heart disease for men and women, 1921-98, England and Wales

Lawlor et al. BMJ 2001

# Índice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# Historia de la epidemiología: Enfermedades crónicas

- Estudio Framingham

# Historia de la epidemiología: Enfermedades crónicas

- Estudio Framingham
  - Más de 1000 artículos publicados
  - Está en su tercera generación
  - Casi todo lo que sabemos sobre la relación del infarto con:
    - Tabaco
    - Colesterol (bueno y el malo)
    - Obesidad
    - Hipertensión

# Historia de la epidemiología:

## Enfermed

- Estudio F

**TABLE 4. Multivariable-Adjusted Relative Risks for CHD According to TC Categories**

| | Men | | Women | |
|---|---|---|---|---|
| | Relative Risk | 95% CI | Relative Risk | 95% CI |
| Age, y | 1.05‡ | 1.04–1.06 | 1.04‡ | 1.03–1.06 |
| Blood pressure | | | | |
| Normal (including optimal) | 1.00 | Referent | 1.00 | Referent |
| High normal | 1.31 | 0.98–1.76 | 1.30 | 0.86–1.98 |
| Hypertension stage I | 1.67† | 1.28–2.18 | 1.73† | 1.19–2.52 |
| Hypertension stage II–IV | 1.84‡ | 1.37–2.49 | 2.12† | 1.42–3.17 |
| Cigarette use (y/n) | 1.68‡ | 1.37–2.06 | 1.47† | 1.12–1.94 |
| Diabetes (y/n) | 1.50* | 1.06–2.13 | 1.77† | 1.16–2.69 |
| TC, mg/dL | | | | |
| <200 | 1.00 | Referent | 1.00 | Referent |
| 200–239 | 1.31* | 1.01–1.68 | 1.51* | 1.01–2.24 |
| ≥240 | 1.90‡ | 1.47–2.47 | 1.72† | 1.15–2.56 |
| HDL-C, mg/dL | | | | |
| <35 | 1.47† | 1.16–1.86 | 2.02† | 1.29–3.15 |
| 35–59 | 1.00 | Referent | 1.00 | Referent |
| ≥60 | 0.56† | 0.37–0.83 | 0.58† | 0.43–0.79 |

The multivariate models were performed separately for men and women. Each model included simultaneously all variables listed in the table. All analyses used categorical variables.

*.01<*P*<.05, †.001<*P*<.01, ‡*P*<.001.

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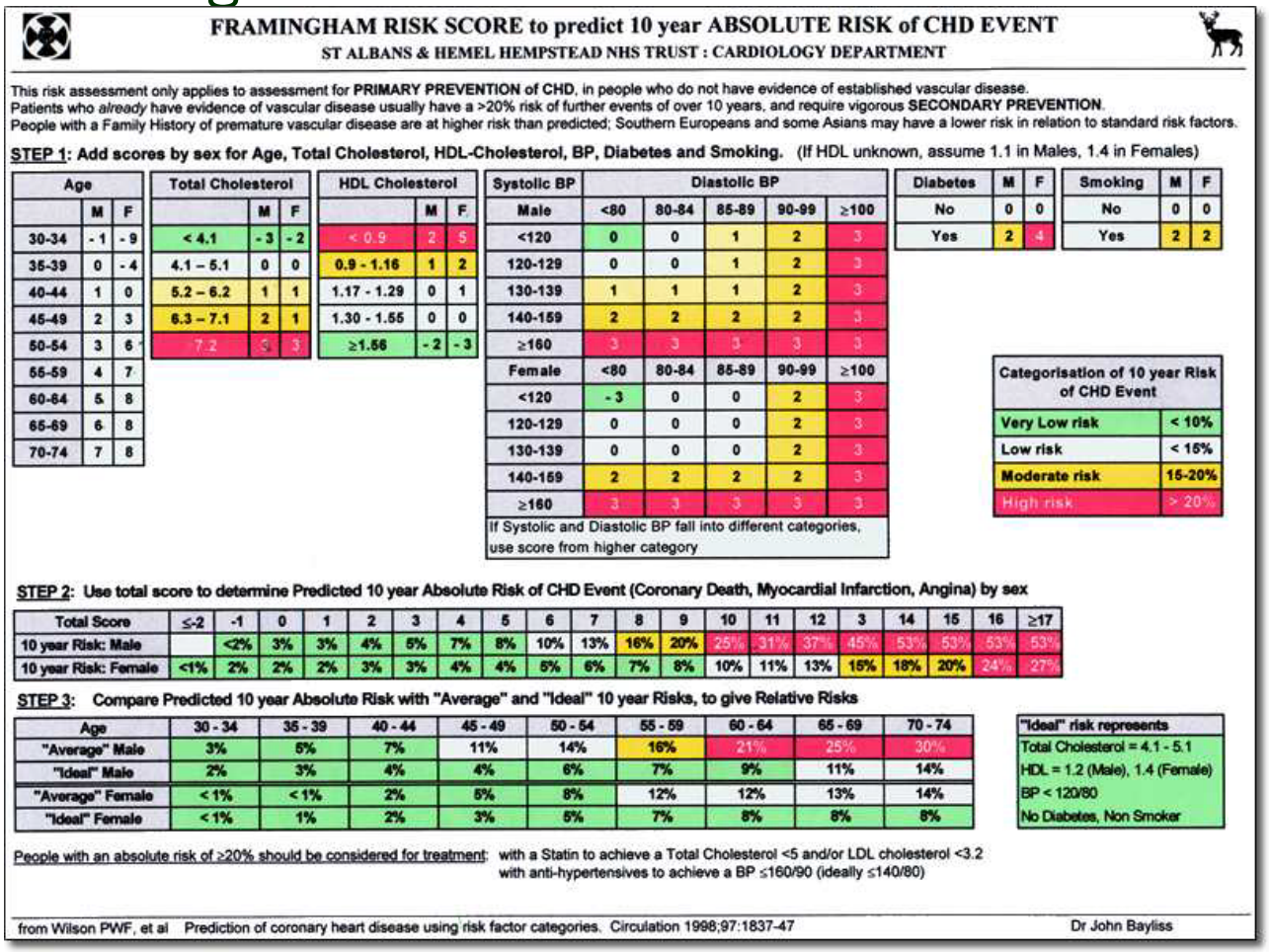
# Historia de la epidemiología: Enfermedades crónicas

- Estudio Framingham



**FRAMINGHAM RISK SCORE to predict 10 year ABSOLUTE RISK of CHD EVENT**

**ST ALBANS & HEMEL HEMPSTEAD NHS TRUST : CARDIOLOGY DEPARTMENT**

This risk assessment only applies to assessment for **PRIMARY PREVENTION of CHD**, in people who do not have evidence of established vascular disease.
Patients who *already* have evidence of vascular disease usually have a >20% risk of further events of over 10 years, and require vigorous **SECONDARY PREVENTION**.
People with a Family History of premature vascular disease are at higher risk than predicted; Southern Europeans and some Asians may have a lower risk in relation to standard risk factors.

**STEP 1: Add scores by sex for Age, Total Cholesterol, HDL-Cholesterol, BP, Diabetes and Smoking.** (If HDL unknown, assume 1.1 in Males, 1.4 in Females)

| Age | M | F |
|---|---|---|
| 30-34 | -1 | -9 |
| 35-39 | 0 | -4 |
| 40-44 | 1 | 0 |
| 45-49 | 2 | 3 |
| 50-54 | 3 | 6 |
| 55-59 | 4 | 7 |
| 60-64 | 5 | 8 |
| 65-69 | 6 | 8 |
| 70-74 | 7 | 8 |

| Total Cholesterol | M | F |
|---|---|---|
| < 4.1 | -3 | -2 |
| 4.1 – 5.1 | 0 | 0 |
| 5.2 – 6.2 | 1 | 1 |
| 6.3 – 7.1 | 2 | 1 |
| 7.2 | 3 | 3 |

| HDL Cholesterol | M | F |
|---|---|---|
| < 0.9 | 2 | 5 |
| 0.9 - 1.16 | 1 | 2 |
| 1.17 - 1.29 | 0 | 1 |
| 1.30 - 1.55 | 0 | 0 |
| ≥1.56 | -2 | -3 |

| Systolic BP | Diastolic BP | | | | |
|---|---|---|---|---|---|
| Male | <80 | 80-84 | 85-89 | 90-99 | ≥100 |
| <120 | 0 | 0 | 1 | 2 | 3 |
| 120-129 | 0 | 0 | 1 | 2 | 3 |
| 130-139 | 1 | 1 | 1 | 2 | 3 |
| 140-159 | 2 | 2 | 2 | 2 | 3 |
| ≥160 | 3 | 3 | 3 | 3 | 3 |
| Female | <80 | 80-84 | 85-89 | 90-99 | ≥100 |
| <120 | -3 | 0 | 0 | 2 | 3 |
| 120-129 | 0 | 0 | 0 | 2 | 3 |
| 130-139 | 0 | 0 | 0 | 2 | 3 |
| 140-159 | 2 | 2 | 2 | 2 | 3 |
| ≥160 | 3 | 3 | 3 | 3 | 3 |

If Systolic and Diastolic BP fall into different categories, use score from higher category

| Diabetes | M | F |
|---|---|---|
| No | 0 | 0 |
| Yes | 2 | 4 |

| Smoking | M | F |
|---|---|---|
| No | 0 | 0 |
| Yes | 2 | 2 |

| Categorisation of 10 year Risk of CHD Event | |
|---|---|
| Very Low risk | < 10% |
| Low risk | < 15% |
| Moderate risk | 15-20% |
| High risk | > 20% |

**STEP 2: Use total score to determine Predicted 10 year Absolute Risk of CHD Event (Coronary Death, Myocardial Infarction, Angina) by sex**

| Total Score | ≤-2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | ≥17 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 year Risk: Male | | <2% | 3% | 3% | 4% | 5% | 7% | 8% | 10% | 13% | 16% | 20% | 25% | 31% | 37% | 45% | 53% | 53% | 53% | 53% |
| 10 year Risk: Female | <1% | 2% | 2% | 2% | 3% | 3% | 4% | 4% | 5% | 6% | 7% | 8% | 10% | 11% | 13% | 15% | 18% | 20% | 24% | 27% |

**STEP 3: Compare Predicted 10 year Absolute Risk with "Average" and "Ideal" 10 year Risks, to give Relative Risks**

| Age | 30 - 34 | 35 - 39 | 40 - 44 | 45 - 49 | 50 - 54 | 55 - 59 | 60 - 64 | 65 - 69 | 70 - 74 |
|---|---|---|---|---|---|---|---|---|---|
| "Average" Male | 3% | 5% | 7% | 11% | 14% | 16% | 21% | 25% | 30% |
| "Ideal" Male | 2% | 3% | 4% | 4% | 6% | 7% | 9% | 11% | 14% |
| "Average" Female | < 1% | < 1% | 2% | 5% | 8% | 12% | 12% | 13% | 14% |
| "Ideal" Female | < 1% | 1% | 2% | 3% | 5% | 7% | 8% | 8% | 8% |

| "Ideal" risk represents |
|---|
| Total Cholesterol = 4.1 - 5.1 |
| HDL = 1.2 (Male), 1.4 (Female) |
| BP < 120/80 |
| No Diabetes, Non Smoker |

People with an absolute risk of ≥20% should be considered for treatment: with a Statin to achieve a Total Cholesterol <5 and/or LDL cholesterol <3.2 with anti-hypertensives to achieve a BP ≤160/90 (ideally ≤140/80)

from Wilson PWF, et al Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837-47 Dr John Bayliss

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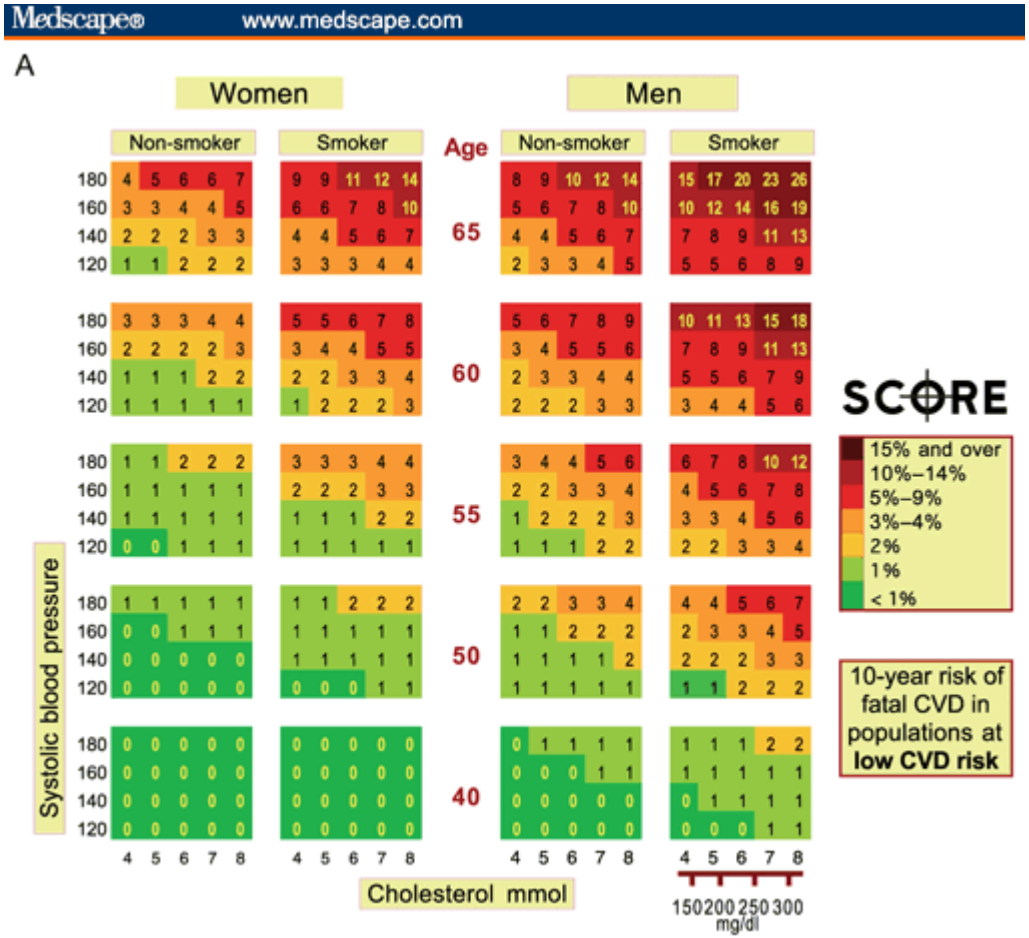
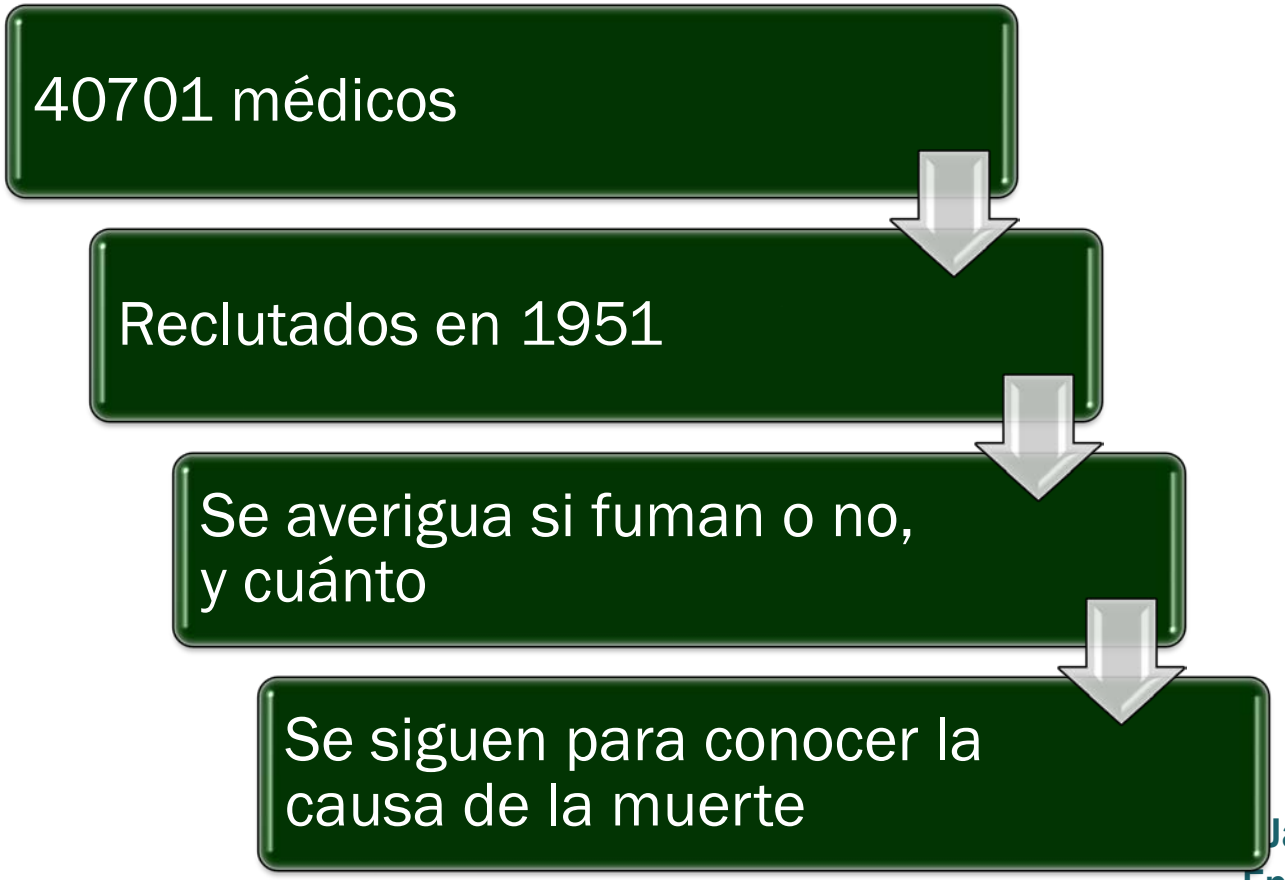
# Historia de la epidemiología: Enfermedades crónicas

- SCORE



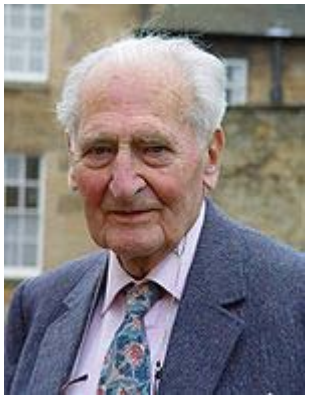
# Historia de la epidemiología: Enfermedades crónicas

- Cohorte de médicos británicos



# Historia de la epidemiología: Enfermedades crónicas

- Cohorte de médicos británicos



  - Richard Doll (1912 – 2005) y Austin Bradford Hill
  - Resultados hasta 2004

  - Primer estudio de seguimiento que estableció la relación entre tabaco y cáncer de pulmón

# Historia de la epidemiología: Enfermedades crónicas

TABLE IV.—*Standardized Death Rate Per Annum Per 1,000 Men Aged 35 Years and Above in Relation to the Most Recent Amount of Tobacco Smoked*

| Cause of Death | No. of Deaths Recorded | Death Rates of Non-smokers | Death Rates of Men Smoking a Daily Average of | | | Death Rate of All Men |
|---|---|---|---|---|---|---|
| | | | 1 g.– | 15 g.– | 25 g. + | |
| Lung cancer | 36* | 0·00 | 0·48 | 0·67 | 1·14 | 0·66 |
| Other cancers | 92 | 2·32 | 1·41 | 1·50 | 1·91 | 1·65 |
| Respiratory disease (other than cancer) | 54 | 0·86 | 0·88 | 1·01 | 0·77 | 0·94 |
| Coronary thrombosis | 235 | 3·89 | 3·91 | 4·71 | 5·15 | 4·27 |
| Other cardiovascular diseases | 126* | 2·23 | 2·07 | 1·58 | 2·78 | 2·14 |
| Other diseases | 247 | 4·27 | 4·67 | 3·91 | 4·52 | 4·36 |
| All causes | 789 | 13·61 | 13·42 | 13·38 | 16·30 | 14·00 |

* 1 case in which lung cancer was recorded as a contributory but not a direct cause of death has been entered in both groups.

# Historia de la epidemiología: Enfermedades crónicas

BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 26 1954

## THE MORTALITY OF DOCTORS IN RELATION TO THEIR SMOKING HABITS

A PRELIMINARY REPORT

BY

RICHARD DOLL, M.D., M.R.C.P.

*Member of the Statistical Research Unit of the Medical Research Council*

AND

A. BRADFORD HILL, C.B.E., F.R.S.

*Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council*

# Historia de la epidemiología: Enfermedades crónicas

Cite this article as: BMJ, doi:10.1136/bmj.38142.554479.AE (published 22 June 2004)

Papers

## Mortality in relation to smoking: 50 years' observations on male British doctors

Richard Doll, Richard Peto, Jillian Boreham, Isabelle Sutherland

# Historia de la epidemiología: Enfermedad

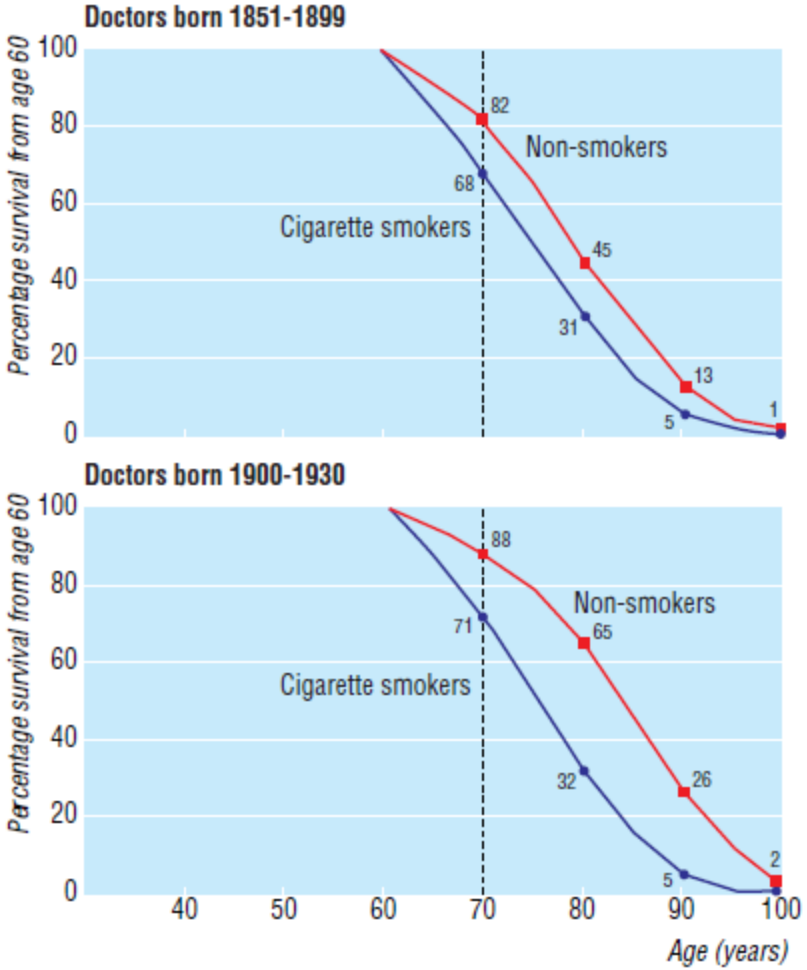



**Fig 1** Survival from age 60 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1851-1899 (median 1889) and 1900-1930 (median 1915), with percentages alive at each decade of age

# Historia de la epidemiol
# Enfermedades crónica

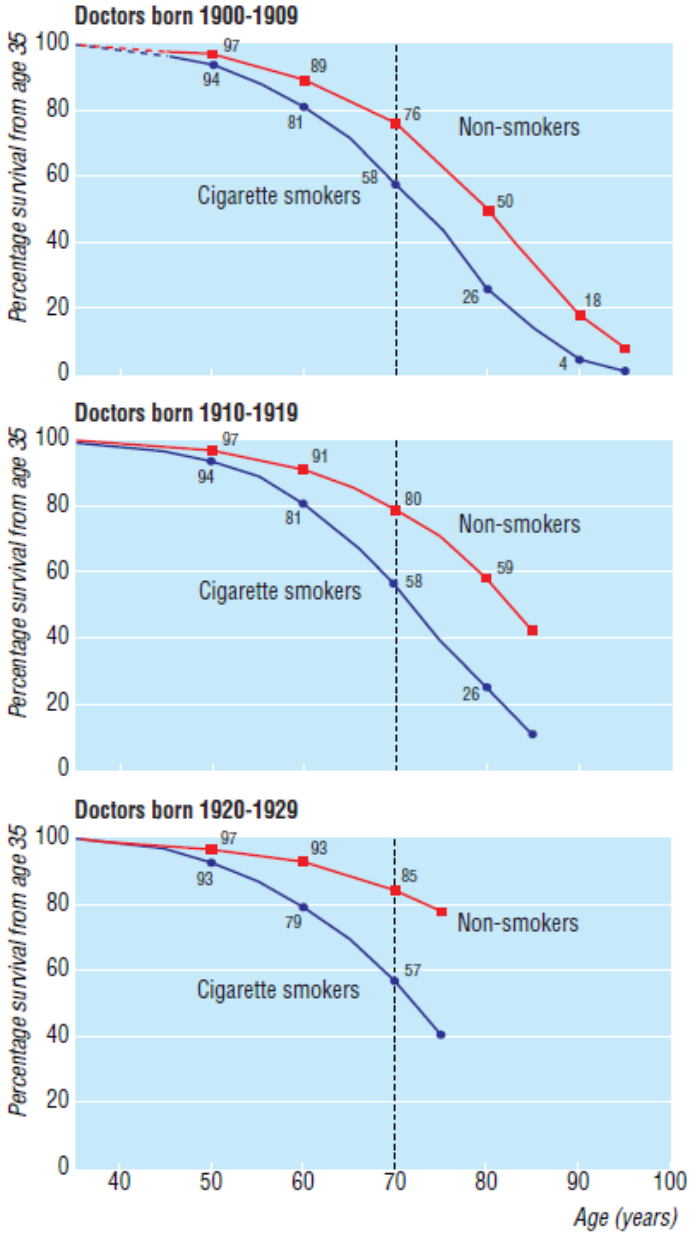



**Fig 2** Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1909, 1910-1919, and 1920-1929, with percentages alive at each decade of age

# Historia de la epidemiología: Enfermedades crónicas

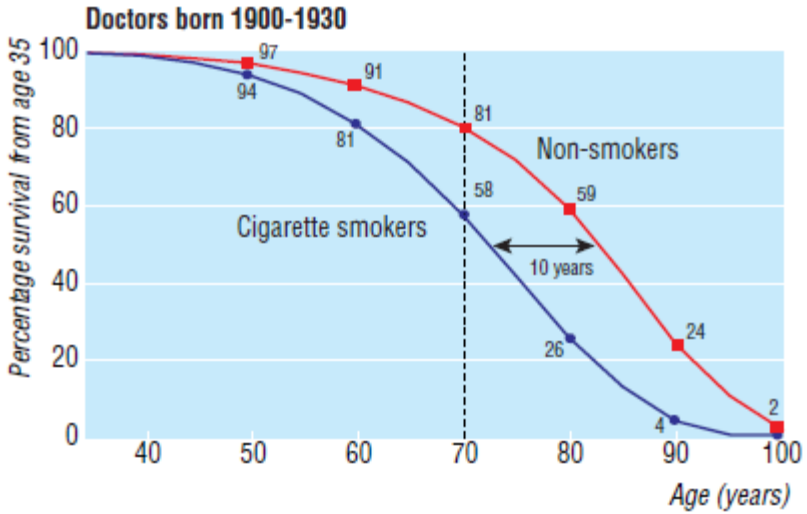



**Fig 3** Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1930, with percentages alive at each decade of age

# Historia de la epidemiología: Enfermedades crónicas

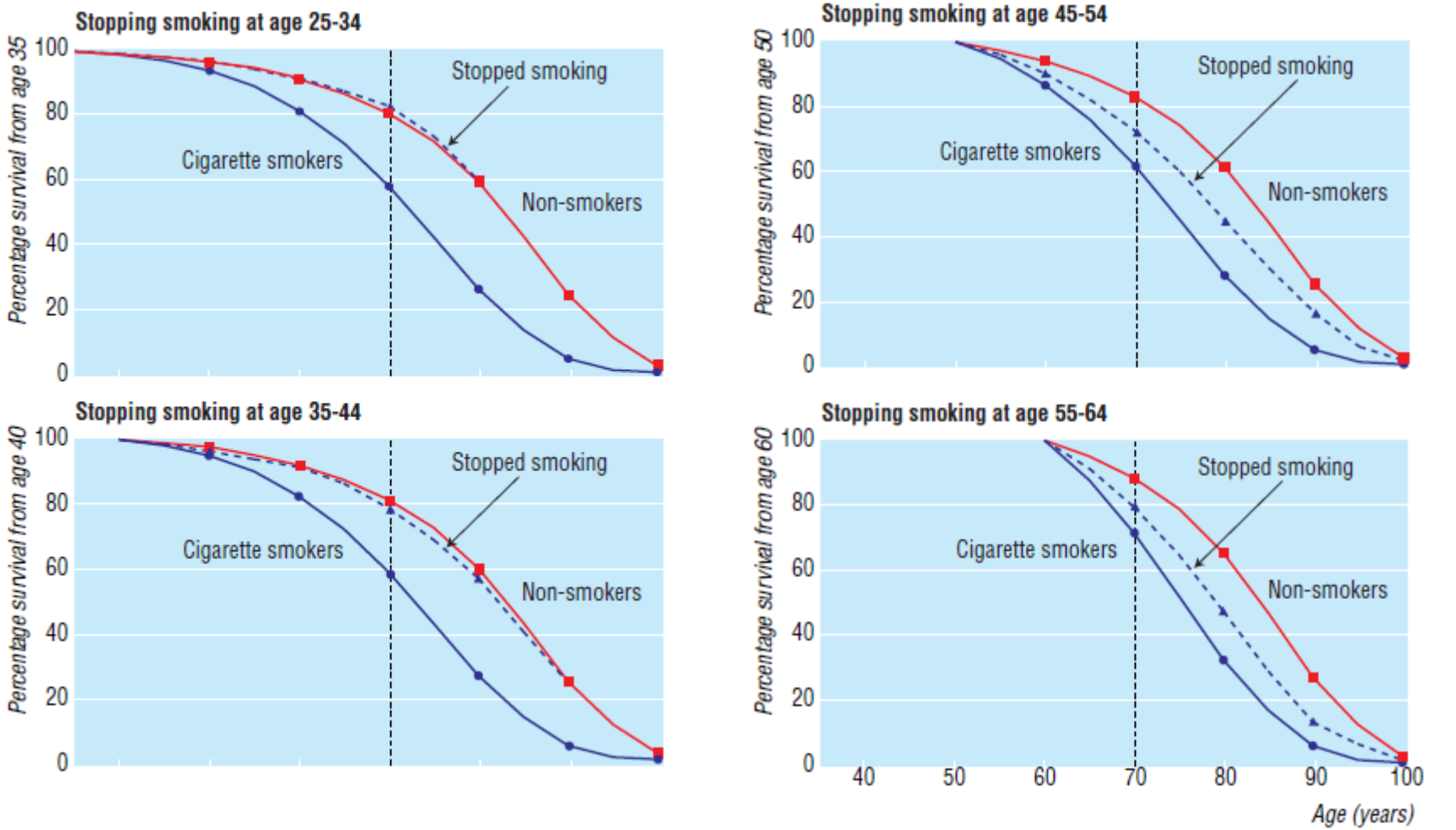



**Fig 4** Effects on survival of stopping smoking cigarettes at age 25-34 (effect from age 35), age 35-44 (effect from age 40), age 45-54 (effect from age 50), and age 55-64 (effect from age 60)

# Historia de la epidemiología: Enfermedades crónicas

- Ancel Keys (1904-2004)

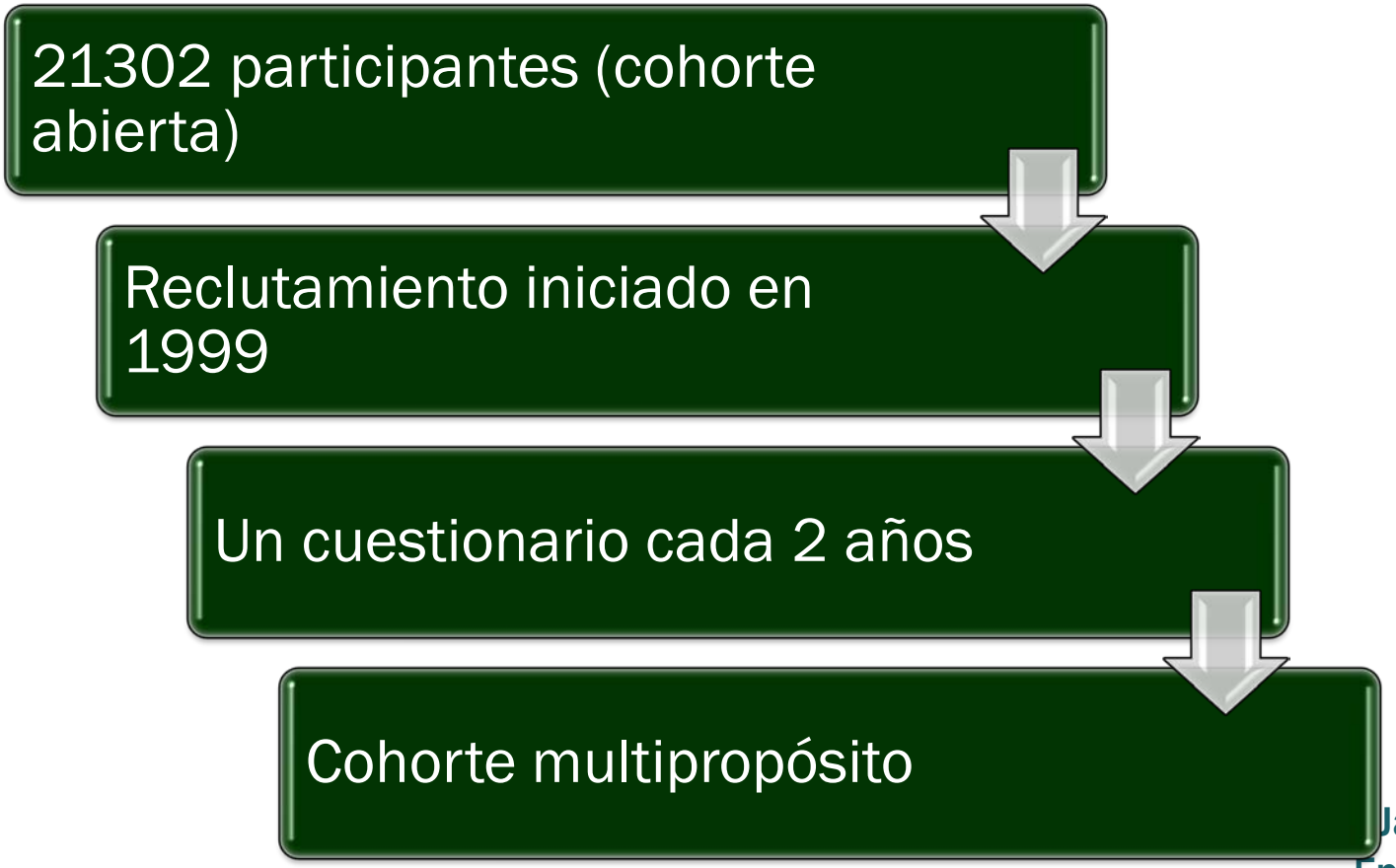


# Historia de la epidemiología: Enfermedades crónicas

- Seven Countries Study

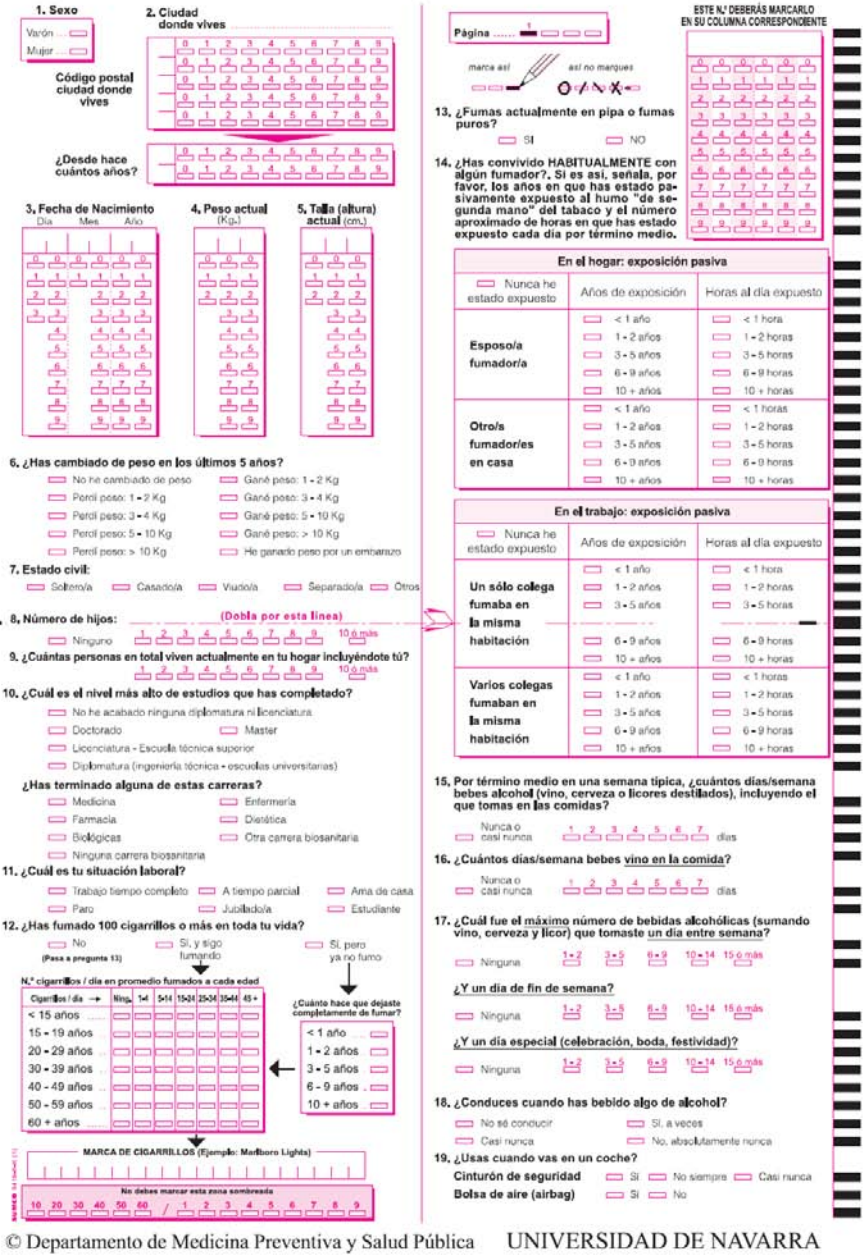
# Historia de la epidemiología: Enfermedades crónicas

- Proyecto SUN



# Historia de la epidemiolo
# Enfermedades crónicas

- Proyecto SUN

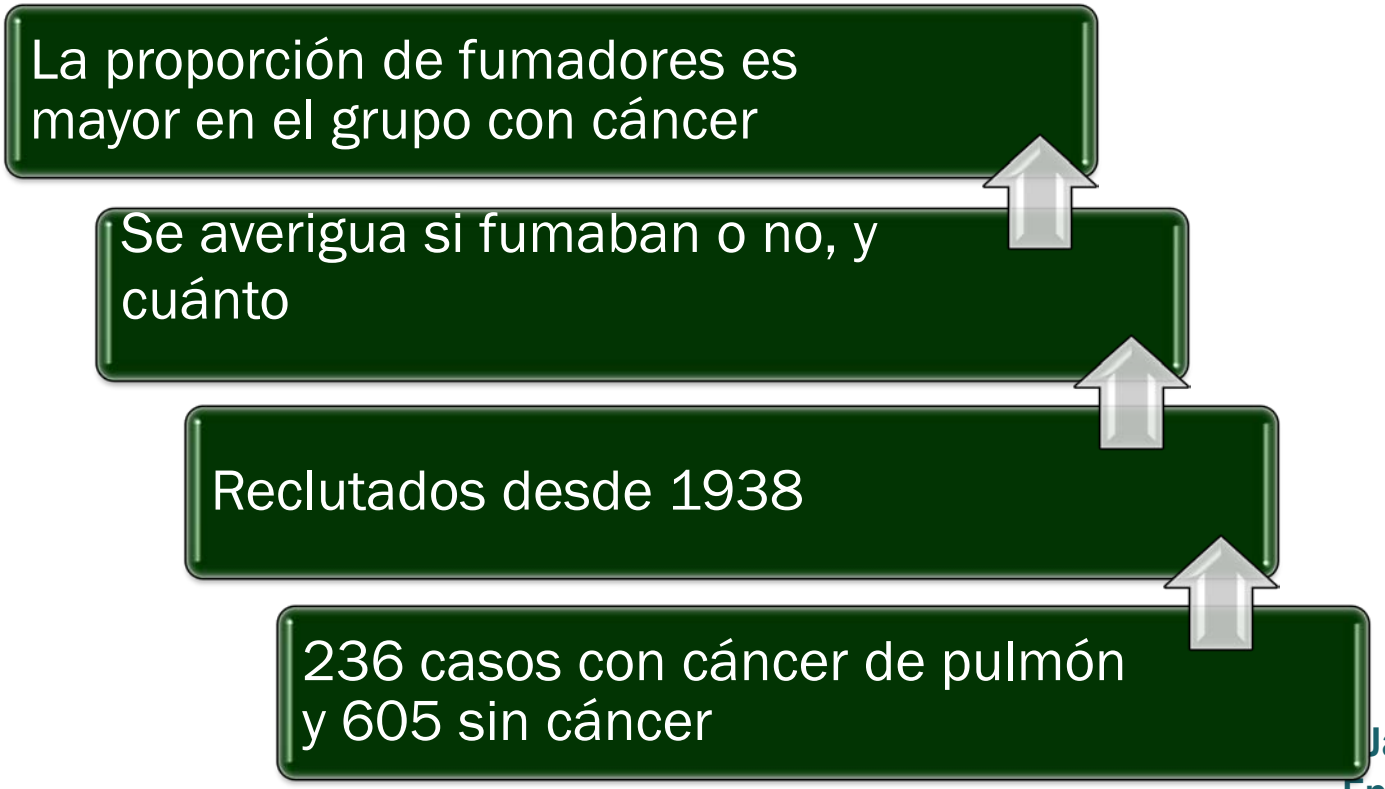


# Historia de la epidemiología: Enfermedades crónicas

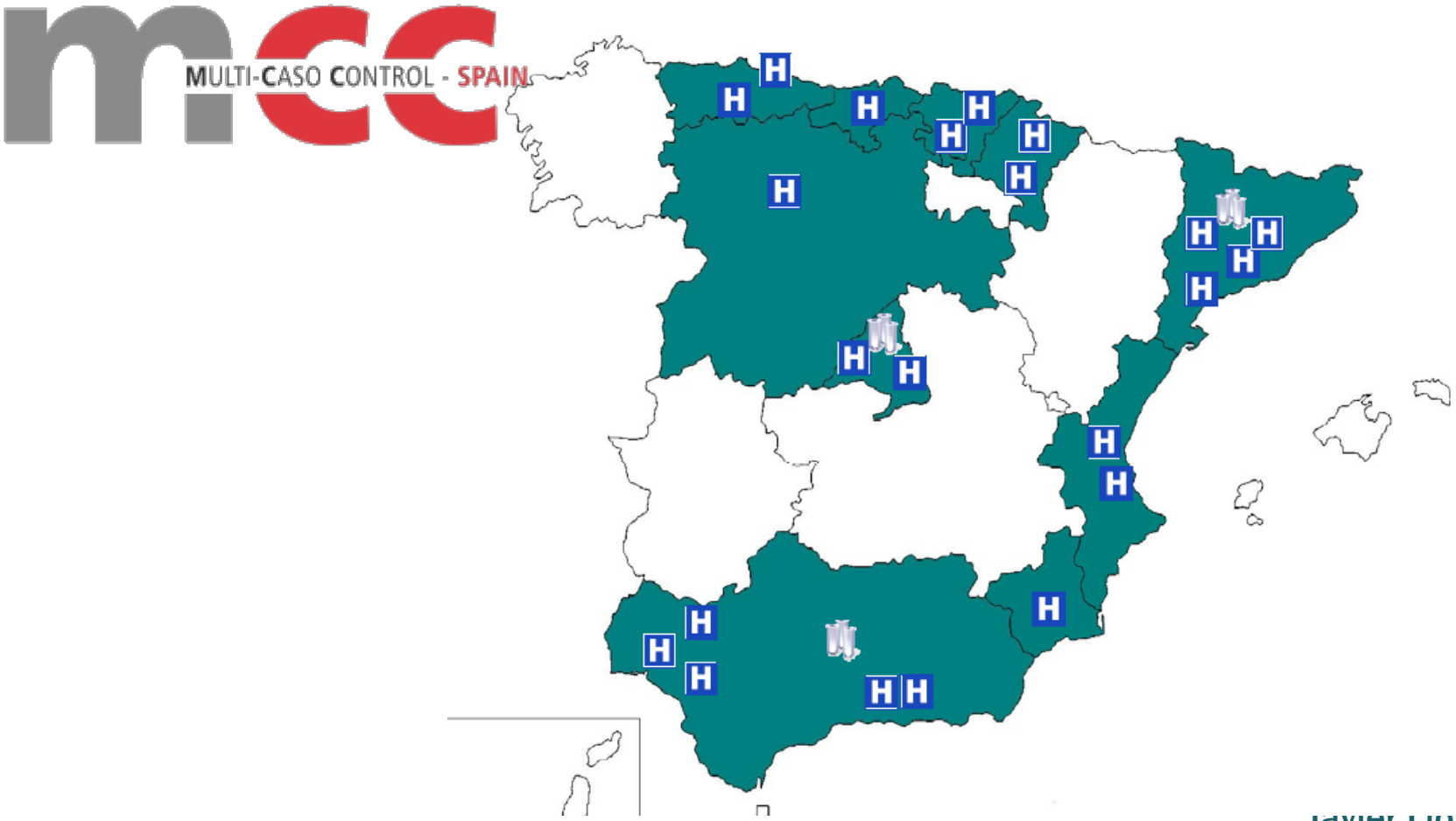
- Estudio de cohortes:
  - Se muestrea a partir de la exposición
  - El efecto es una variable con distribución binomial
  - Si se tiene en cuenta el tiempo: distribución de Poisson

# Historia de la epidemiología: Enfermedades crónicas

- Estudios de casos y controles (1950)
- Morton Levin (1904 – 1995)



# Historia de la epidemiología: Enfermedades crónicas



# Historia de la epidemiología: Enfermedades crónicas

MULTI-CASO CONTROL - SPAIN

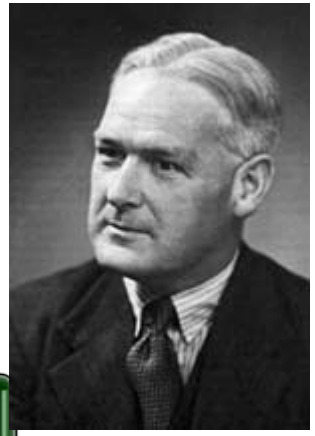
| | CONTROL | COLON | MAMA | PRÓSTATA | ESTÓMAGO | LEUCEMIA | TOTAL |
|---|---|---|---|---|---|---|---|
| Asturias | 219 | 84 | 102 | 17 | 15 | 55 | 492 |
| Barcelona | 828 | 719 | 301 | 404 | 104 | 349 | 2705 |
| Cantabria | 253 | 144 | 135 | 163 | 24 | 26 | 745 |
| Gipuzkoa | 362 | 127 | 229 | | | | 718 |
| Granada | 184 | 136 | | 67 | 5 | 35 | 427 |
| Huelva | 104 | 49 | 49 | 92 | 13 | | 307 |
| León | 316 | 403 | 222 | | 126 | | 1067 |
| Madrid | 698 | 251 | 359 | 321 | 122 | | 1751 |
| Murcia | 44 | 41 | | | 4 | | 89 |
| Navarra | 274 | 125 | 228 | | 59 | | 686 |
| Valencia | 115 | 56 | 35 | 76 | 11 | 2 | 295 |
| TOTAL | 3397 | 2135 | 1660 | 1140 | 483 | 467 | 9282 |

# Historia de la epidemiología: Enfermedades crónicas

- Estudios de casos y controles
  - Se muestra de dos poblaciones (enfermos y no enfermos)
  - La distribución de fondo es hipergeométrica

# Historia de la epidemiología: Enfermedades crónicas

- Ensayo clínico (1948)
- Austin Bradford Hill (1897 – 1991)



107 enfermos de tuberculosis que no podían recibir otro tratamiento

Reclutados en 1947

Se distribuyen **al azar** en dos grupos

55 reciben estreptomicina y hacen reposo en cama

52 hacen reposo en cama

# Historia de la epidemiología: Enfermedades crónicas

- Ensayo clínico

TABLE II.—*Assessment of Radiological Appearance at Six Months as Compared with Appearance on Admission*

| Radiological Assessment | Streptomycin Group | | Control Group | |
|---|---|---|---|---|
| Considerable improvement .. | 28 | *51%* | 4 | *8%* |
| Moderate or slight improvement | 10 | *18%* | 13 | *25%* |
| No material change .. .. | 2 | *4%* | 3 | *6%* |
| Moderate or slight deterioration | 5 | *9%* | 12 | *23%* |
| Considerable deterioration .. | 6 | *11%* | 6 | *11%* |
| Deaths .. .. .. .. | 4 | *7%* | 14 | *27%* |
| Total .. .. | 55 | *100%* | 52 | *100%* |

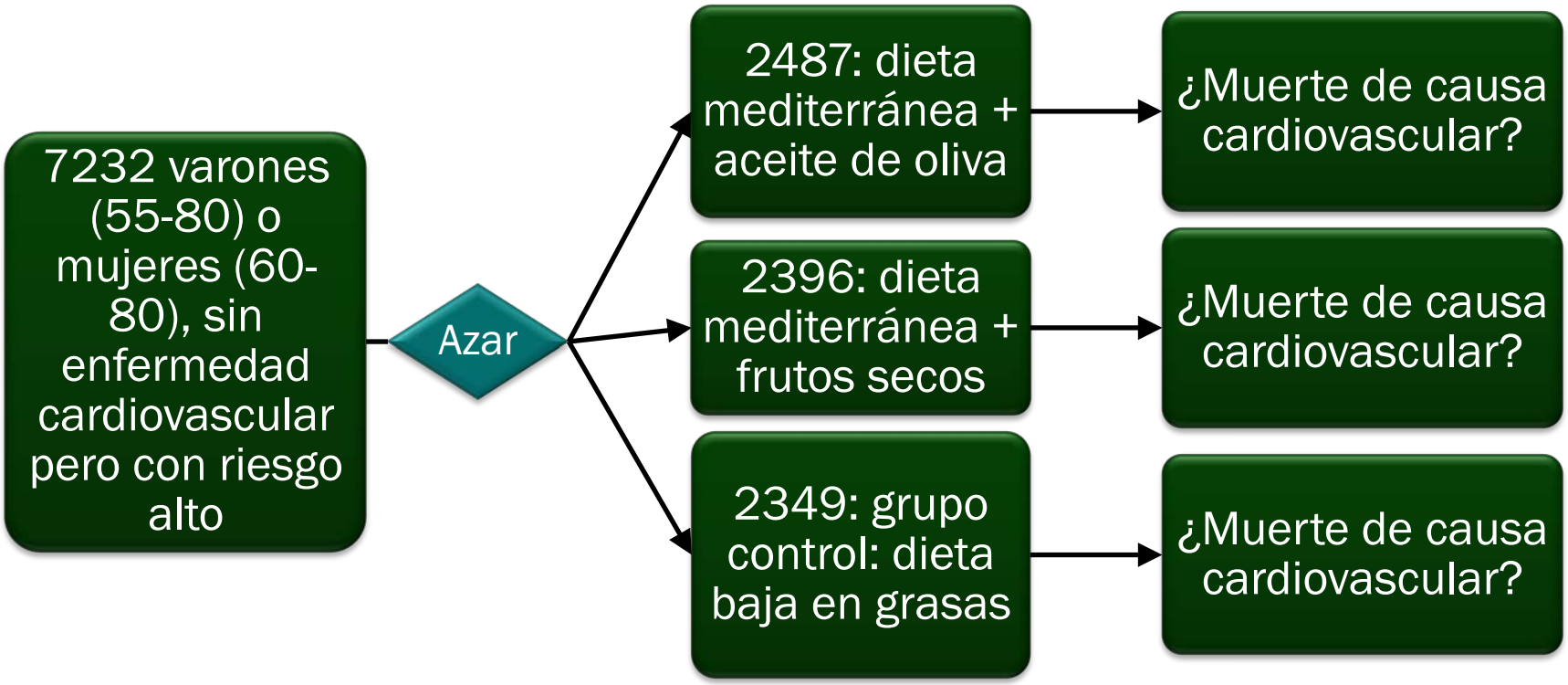
# Historia de la epidemiología: Enfermedades crónicas

*"Before deducing 'causation' and taking action we shall not invariably have to sit around awaiting the results of the research. The whole chain may have to be unraveled or a few links may suffice. It will depend upon circumstances."*

*Austin B. Hill*

# Historia de la epidemiología: Enfermedades crónicas

- Estudio Predimed



# Historia de la epidemiología: Enfermedades crónicas

- Estudios largos
- No se busca un agente sino varios factores que influyan en la aparición de la enfermedad (**factores de riesgo**)
- Medidas de prevención:
  - Cambios de estilo de vida
  - Eliminar el agente (p.e.: tabaco, asbesto)
  - Cambios en el ambiente

# Índice


- De las epidemias de cólera...
- Fases en el desarrollo de la epidemiología
- Tipos de estudio
- **Herramientas de cálculo en la epidemiología actual**
- ¿Para qué sirve la epidemiología?
- Nuestros problemas actuales
- ... hasta la crisis de los pepinos

# Herramientas estadísticas en la Epi de hoy

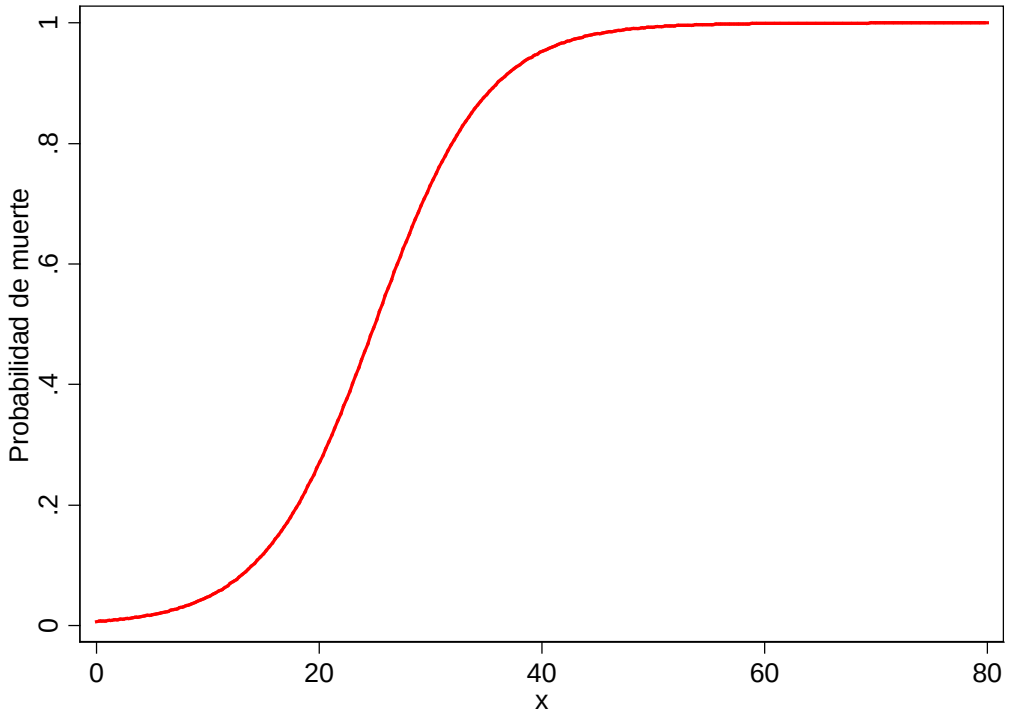
- Efecto binario (sí / no): regresión logística

$$\ln \frac{p}{1-p} = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3$$

# Herramientas estadísticas en la Epi de hoy

- Efecto binario (sí / no): **regresión logística**

$$\ln \frac{p}{1-p} = \alpha + \beta_1 x_1$$



# Herramientas estadísticas en la Epi de hoy

- Regresión de Poisson:
- Variable dependiente:
  - Número de casos de infarto en un año
  - Número de infecciones en cada colegio
  - Número de desintegraciones por hora en una masa radioactiva

$$\ln(y) = \ln(N) + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3$$

$N =$ nº de habitantes, nº de alumnos, nº de átomos

# Herramientas estadísticas en la Epi de hoy

- Regresión de Cox:
- Variable dependiente:
  - Tiempo hasta la muerte
  - Tiempo hasta el primer infarto
  - Tiempo hasta aprobar epidemiología

$$\ln(\lambda_t) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3$$

$\lambda_t$ = tasa instantánea de…(enfermar/morir/…) en el tiempo t

# Herramientas estadísticas en la Epi de hoy

## Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial

George D Demetri, Allan T van Oosterom, Christopher R Garrett, Martin E Blackstein, Manisha H Shah, Jaap Verweij, Grant McArthur, Ian R Judson, Michael C Heinrich, Jeffrey A Morgan, Jayesh Desai, Christopher D Fletcher, Suzanne George, Carlo L Bello, Xin Huang, Charles M Baum, Paolo G Casali

*Lancet* 2006; 368: 1329–38

# Herramientas estadísticas en la Epi de hoy

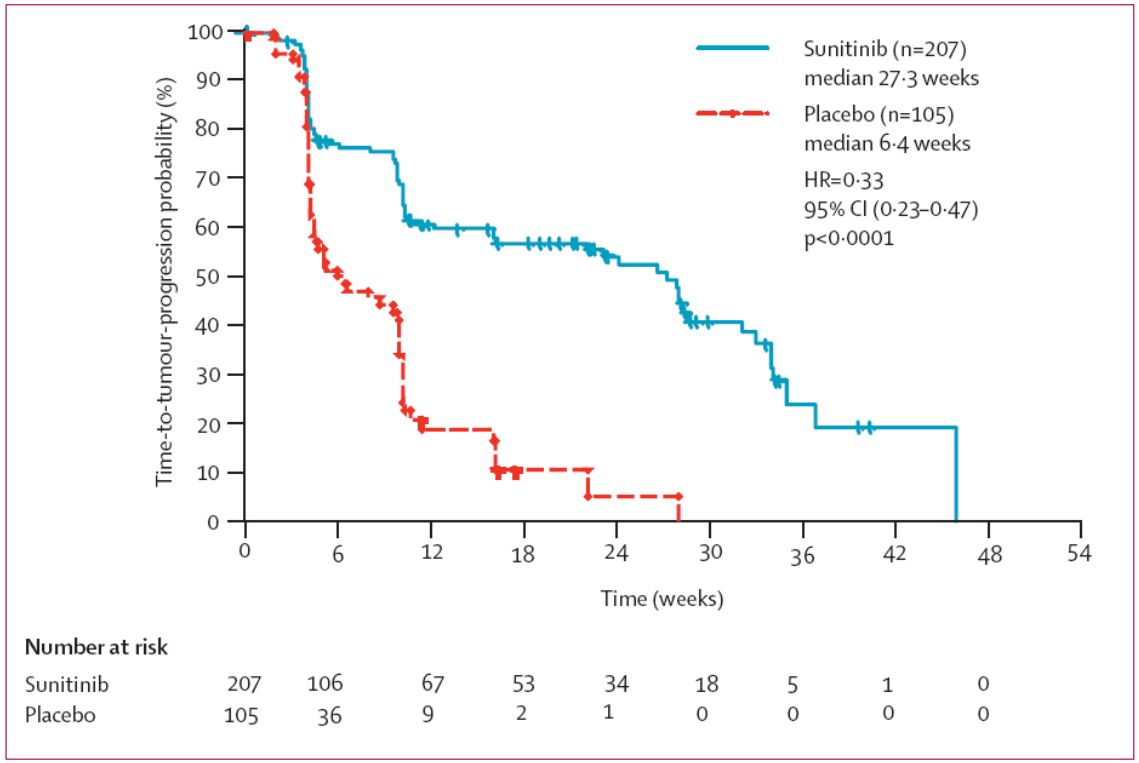



***Figure 2:*** **Kaplan-Meier estimates of time to tumour progression**
Results represent central radiology assessment of ITT population.

# Índice

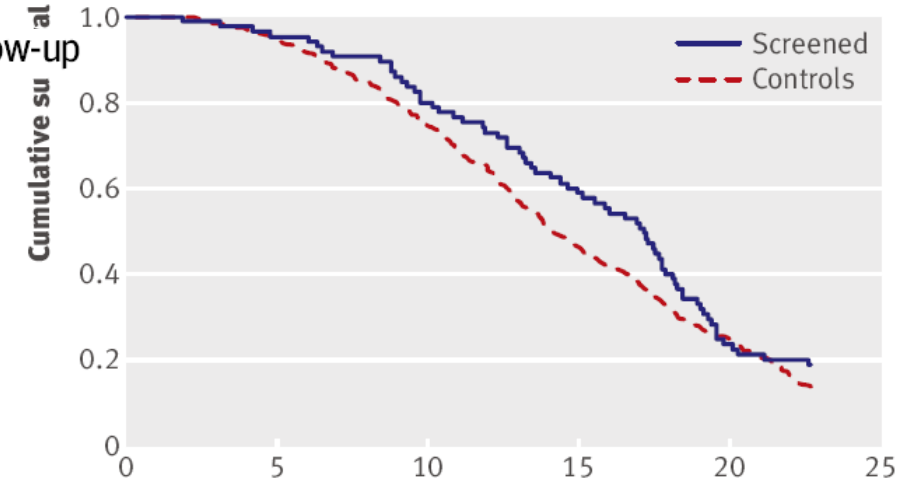

- De las epidemias de cólera…
- Fases en el desarrollo de la epidemiología
- Tipos de estudio
- Herramientas de cálculo en la epidemiología actual
- **¿Para qué sirve la epidemiología?**
- Nuestros problemas actuales
- … hasta la crisis de los pepinos

# ¿Para qué sirve la epidemiología?

- Valorar los métodos diagnósticos

Randomised prostate cancer screening trial: 20 year follow-up

**Sandblom et al. BMJ (2011)**




**Men at risk:**

| | | | | |
|---|---|---|---|---|
| Screened | 81 | 68 | 50 | 20 |
| Controls | 275 | 216 | 135 | 72 |

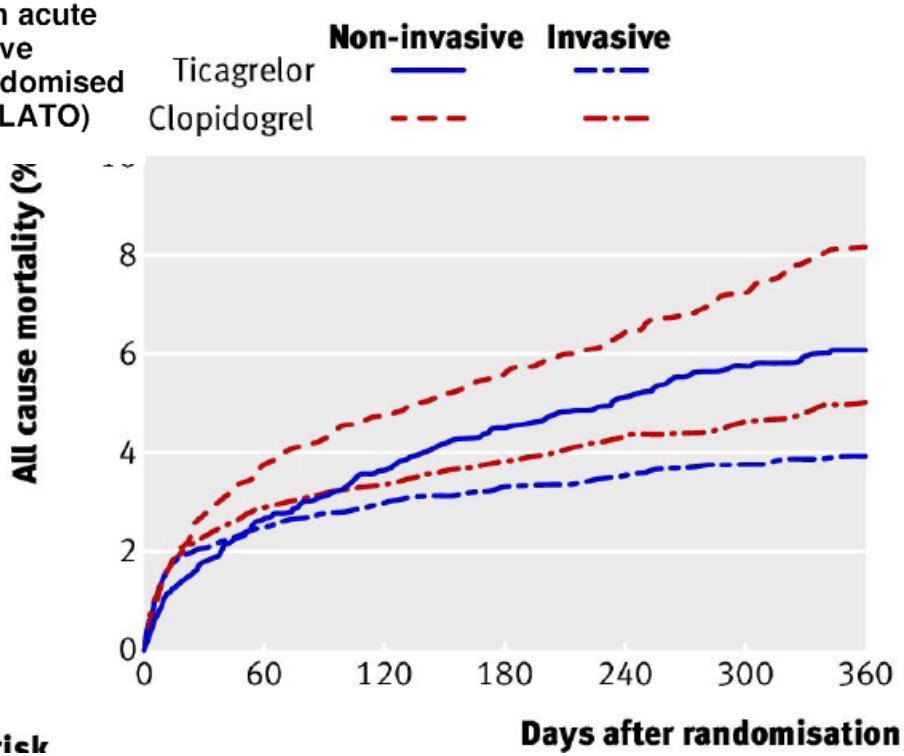
**Fig 2** | Kaplan-Meier curves of overall survival for men diagnosed with prostate cancer in control group (n=292) and screened group (n=85). Log rank test P=0.14

# ¿Para qué sirve la epidemiología?

- Valorar los métodos de tratamiento

**Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATelet inhibition and patient Outcomes (PLATO) trial**

**James et al. BMJ (2011)**

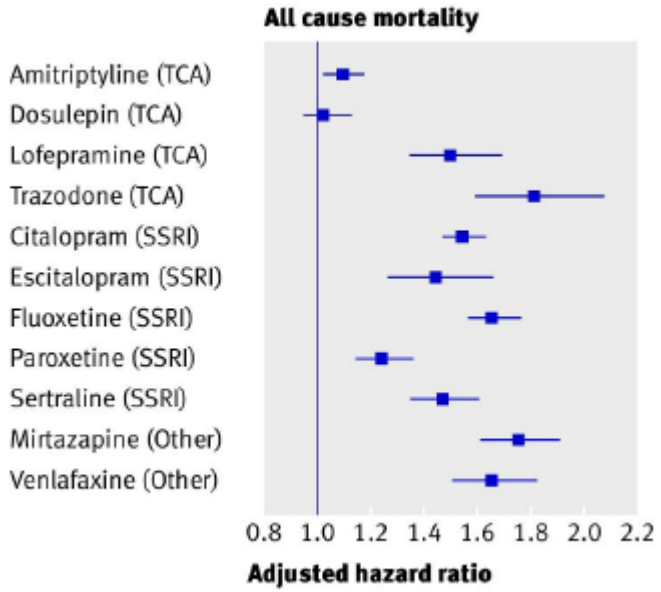


# ¿Para qué sirve la epidemiología?

- Valorar los métodos de tratamiento

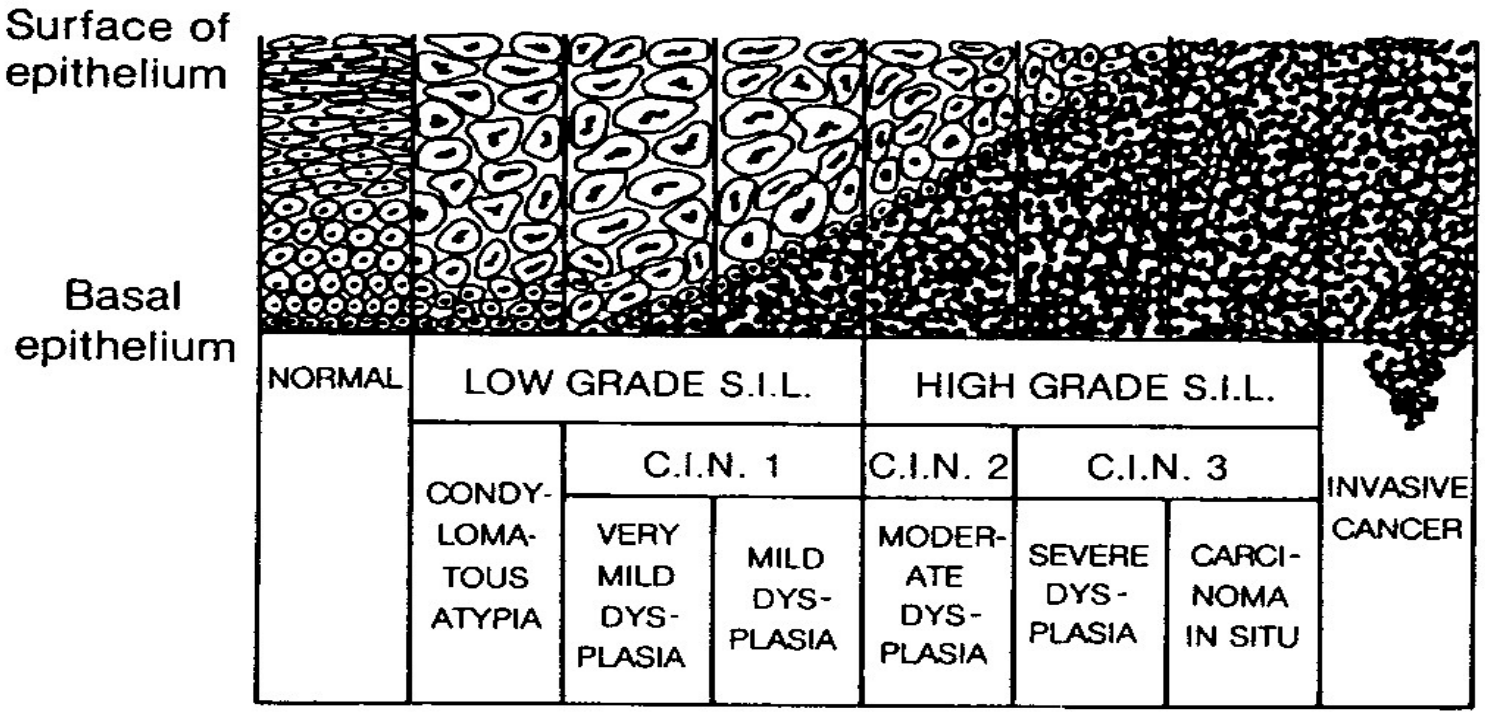
**Antidepressant use and risk of adverse outcomes in older people: population based cohort study**

**Coupland et al, BMJ (2011)**



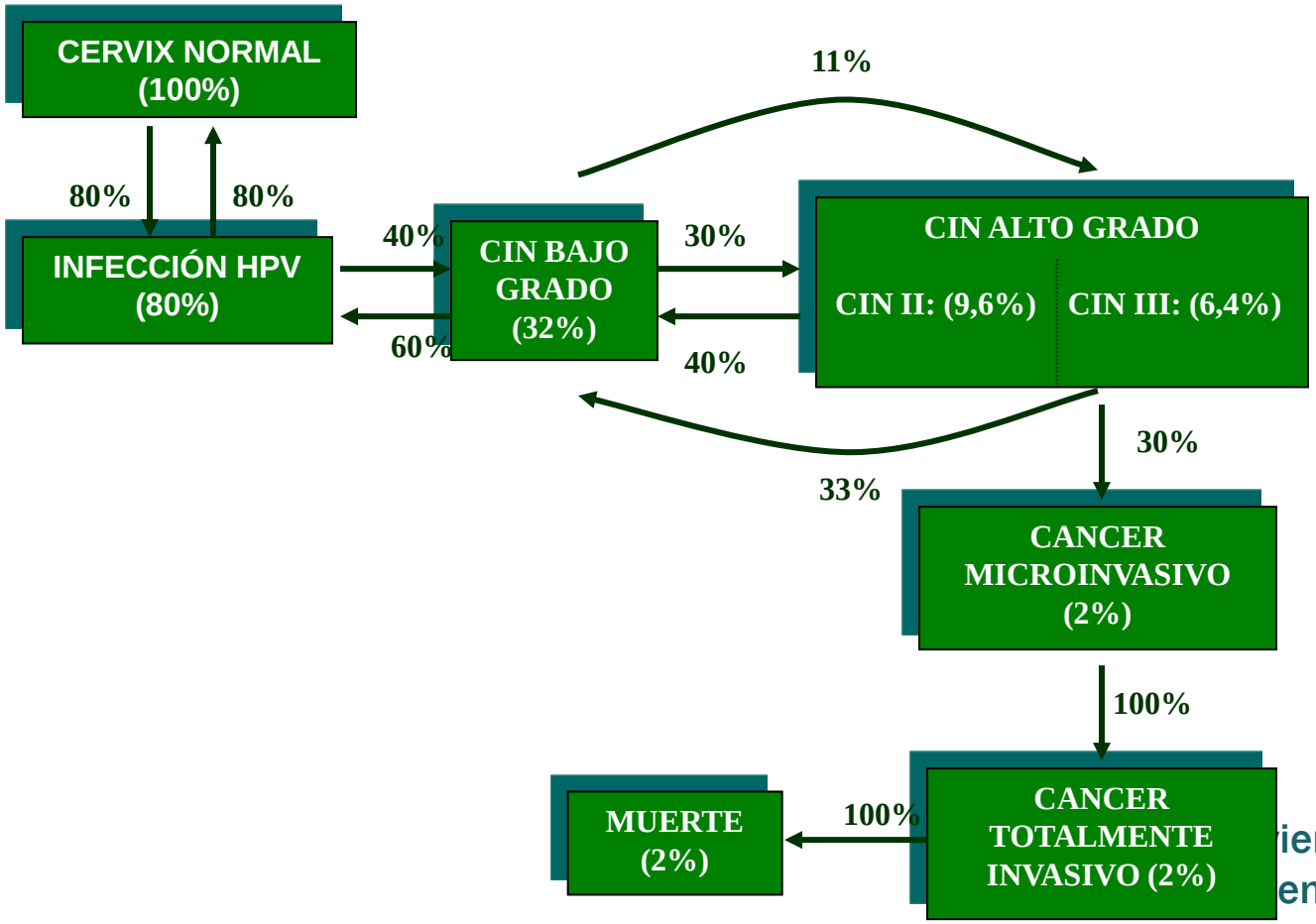
# ¿Para qué sirve la epidemiología?

- Conocer la historia natural de la enfermedad



# ¿Para qué sirve la epidemiología?

- Conocer la historia natural de la enfermedad

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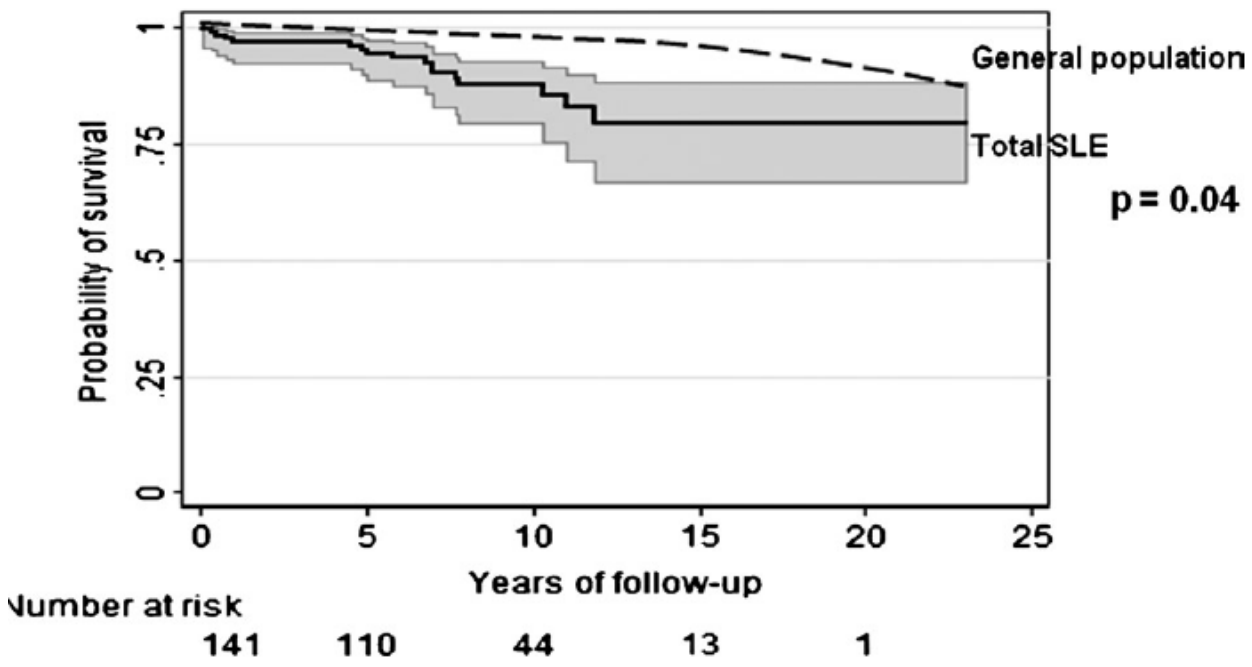
# ¿Para qué sirve la epidemiología?

- Investigar los factores que influyen en el pronóstico

Systemic Lupus Erythematosus in Northwestern Spain

*A 20-Year Epidemiologic Study*

**Alonso et al, Medicine (2011)**



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# Problemas actuales

# Problemas actuales

- Confundir correlación con causa

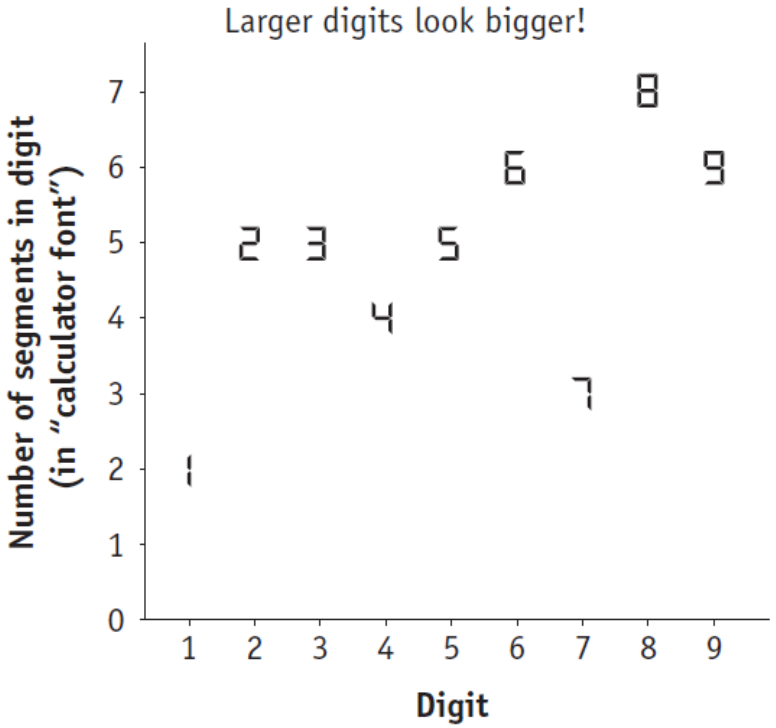
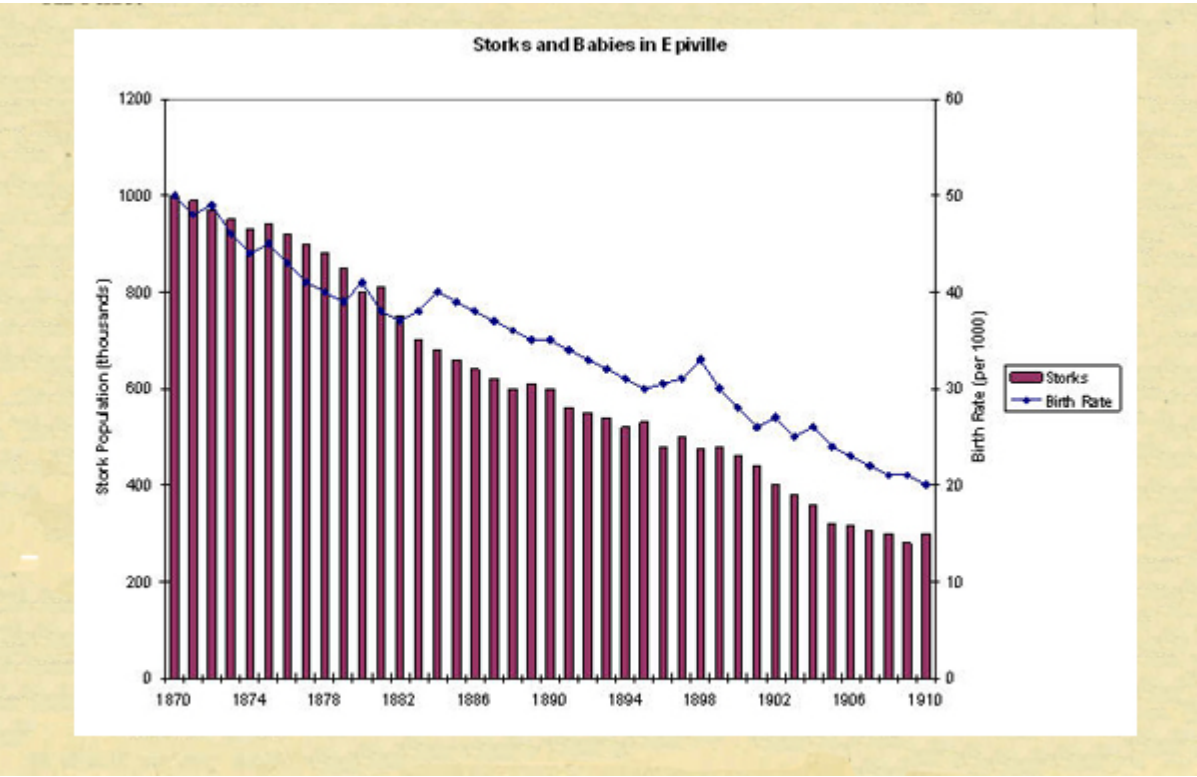



Figure 1. Physical size of the digits 1–9

Javier Llorca.
Epidemiología

# Problemas actuales

- Confundir correlación con causa

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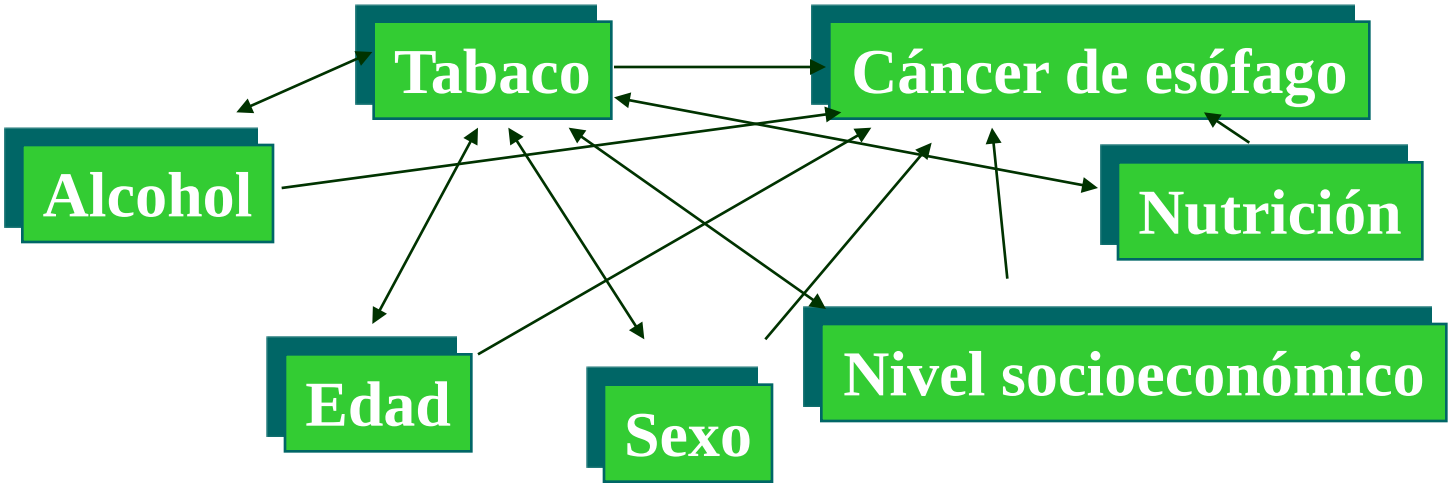
# Problemas actuales

- Sesgo de confusión

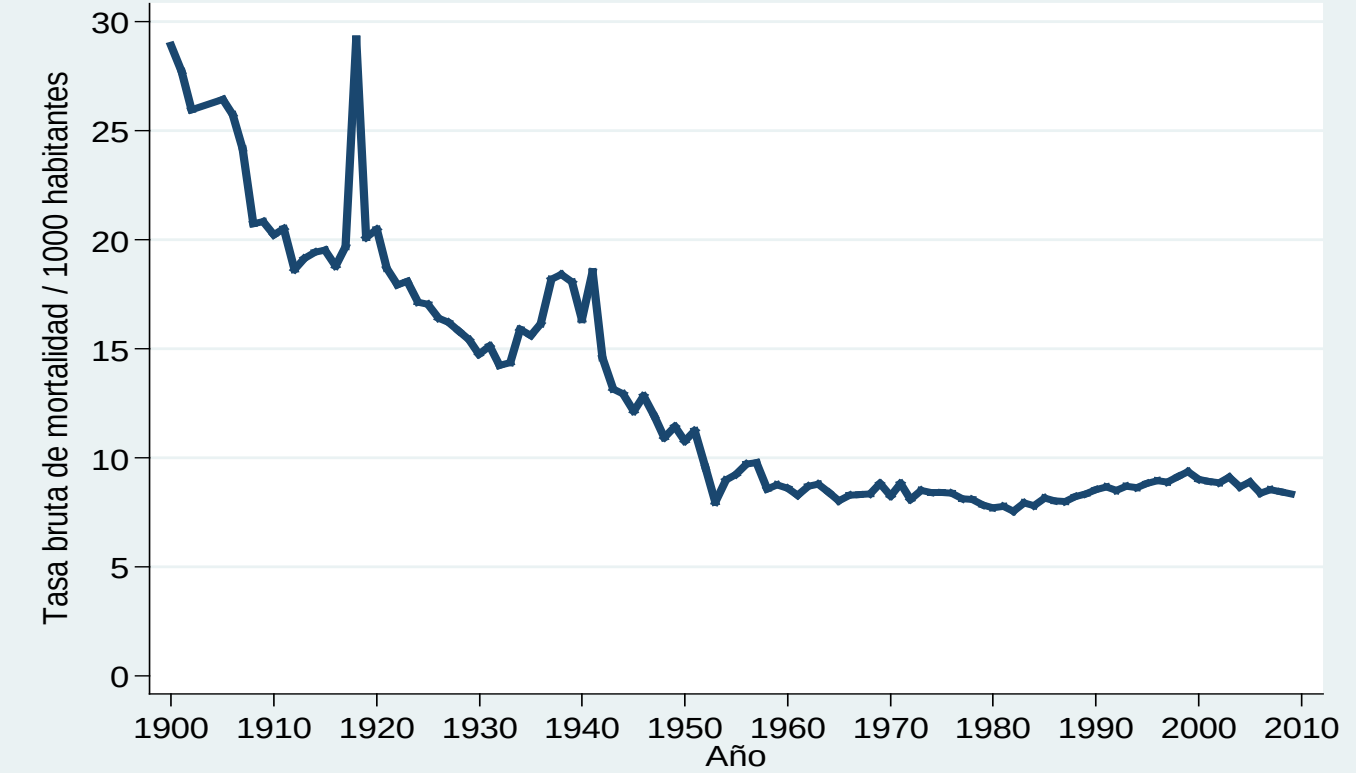
# Problemas actuales

- Sesgo de confusión



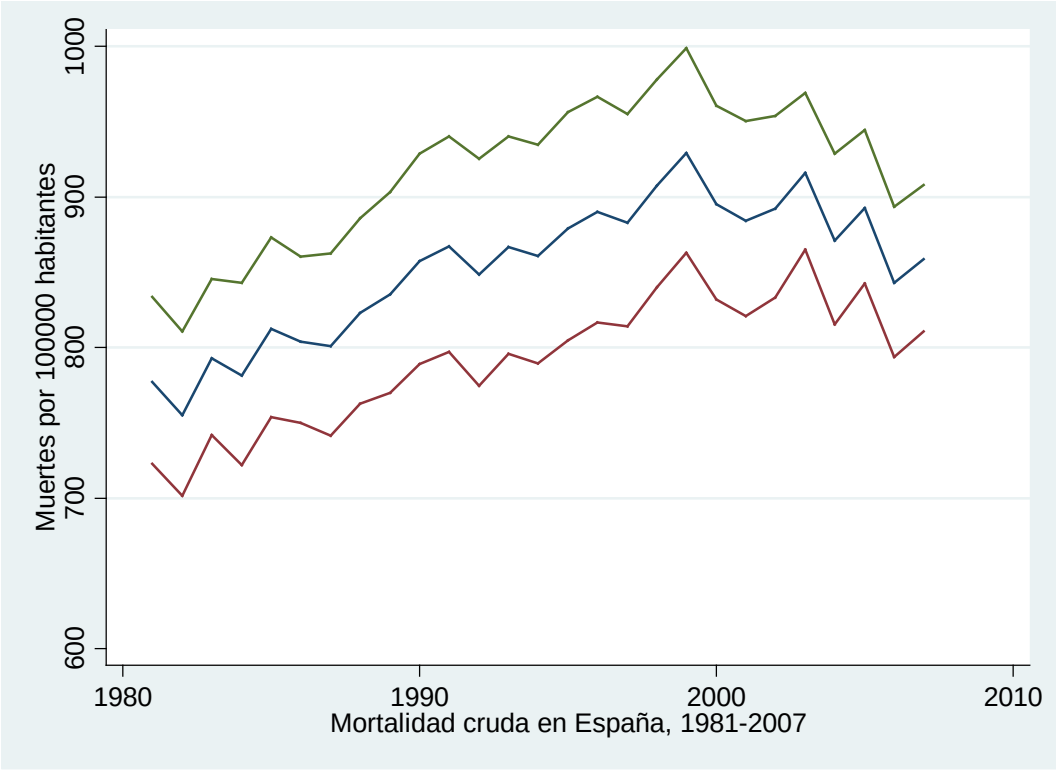
# Problemas actuales

- Sesgo de confusión



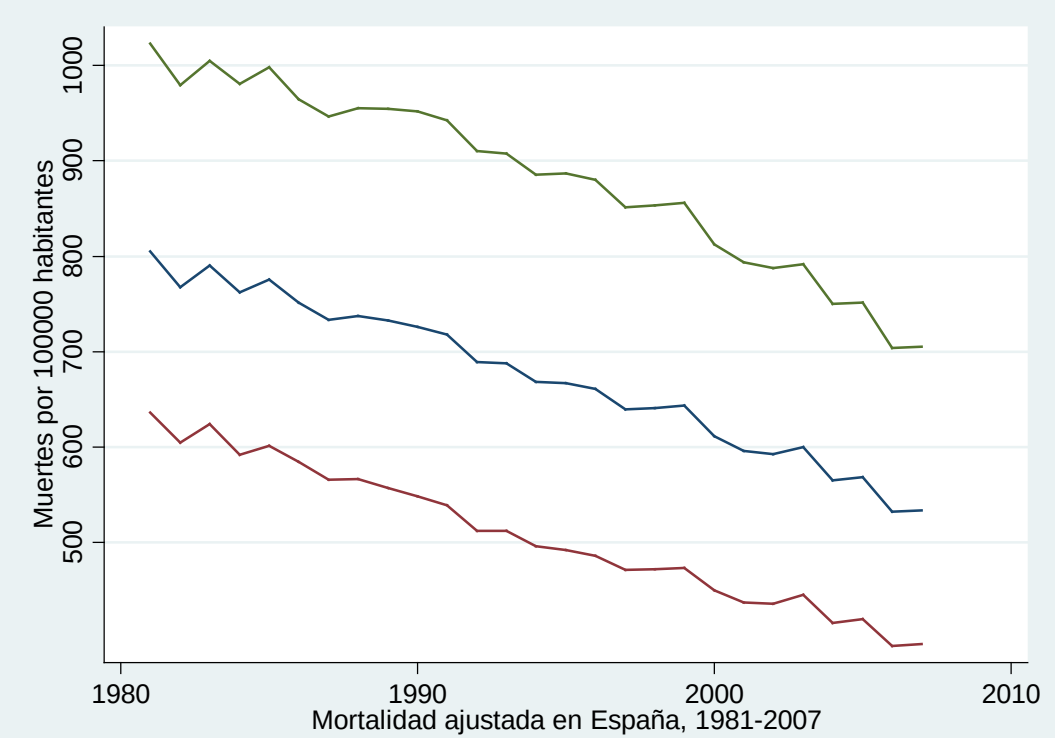
# Problemas actuales

- Sesgo de confusión



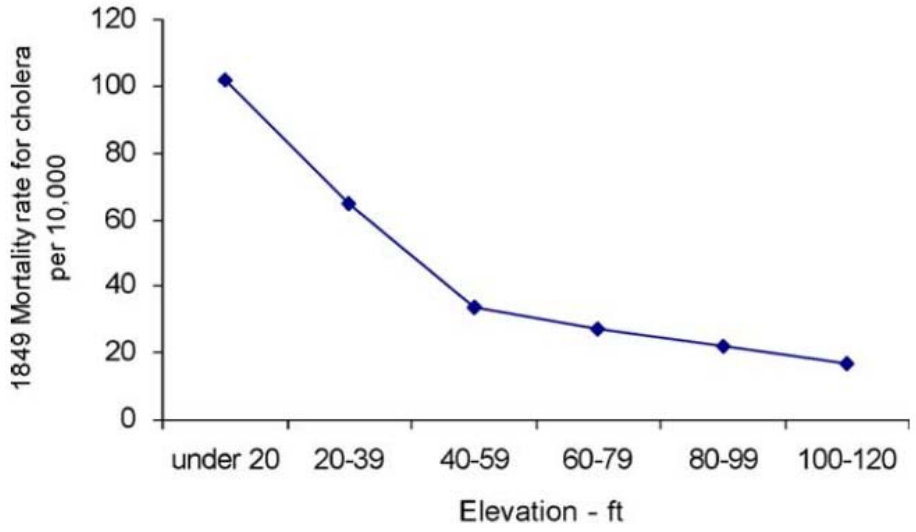
# Problemas actuales

- Sesgo de confusión



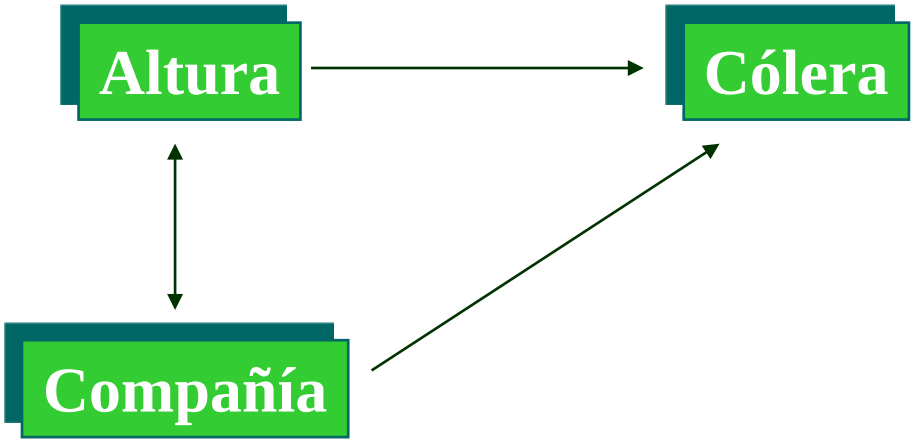
# Historia de la epidemiología: Estadísticas sanitarias (hasta 1850)

- William Farr (1807 – 1883)



# Problemas actuales

- Sesgo de confusión



# Problemas actuales

- Grandes masas de datos y test clásicos

Vol 445|22 February 2007|doi:10.1038/nature05616 nature

ARTICLES

## A genome-wide association study identifies novel risk loci for type 2 diabetes

# Problemas actuales

Type 2 diabetes mellitus results from the interaction of environmental factors with a combination of genetic variants, most of which were hitherto unknown. A systematic search for these variants was recently made possible by the development of high-density arrays that permit the genotyping of hundreds of thousands of polymorphisms. We tested 392,935 single-nucleotide polymorphisms in a French case–control cohort. Markers with the most significant difference in genotype frequencies between cases of type 2 diabetes and controls were fast-tracked for testing in a second cohort. This identified four loci containing variants that confer type 2 diabetes risk, in addition to confirming the known association with the *TCF7L2* gene. These loci include a non-synonymous polymorphism in the zinc transporter *SLC30A8*, which is expressed exclusively in insulin-producing β-cells, and two linkage disequilibrium blocks that contain genes potentially involved in β-cell development or function (*IDE–KIF11–HHEX* and *EXT2–ALX4*). These associations explain a substantial portion of disease risk and constitute proof of principle for the genome-wide approach to the elucidation of complex genetic traits.

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# Problemas actuales

**Table 1 | Confirmed association results**

| SNP | Chromosome | Position (nucleotides) | Risk allele | Major allele | MAF (case) | MAF (ctrl) | Odds ratio (het) | Odds ratio (hom) | Nearest gene |
|---|---|---|---|---|---|---|---|---|---|
| rs7903146 | 10 | 114,748,339 | T | C | 0.406 | 0.293 | 1.65 ± 0.19 | 2.77 ± 0.50 | *TCF7L2* |
| rs13266634 | 8 | 118,253,964 | C | C | 0.254 | 0.301 | 1.18 ± 0.25 | 1.53 ± 0.31 | *SLC30A8* |
| rs1111875 | 10 | 94,452,862 | G | G | 0.358 | 0.402 | 1.19 ± 0.19 | 1.44 ± 0.24 | *HHEX* |
| rs7923837 | 10 | 94,471,897 | G | G | 0.335 | 0.377 | 1.22 ± 0.21 | 1.45 ± 0.25 | *HHEX* |
| rs7480010 | 11 | 42,203,294 | G | A | 0.336 | 0.301 | 1.14 ± 0.13 | 1.40 ± 0.25 | LOC387761 |
| rs3740878 | 11 | 44,214,378 | A | A | 0.240 | 0.272 | 1.26 ± 0.29 | 1.46 ± 0.33 | *EXT2* |
| rs11037909 | 11 | 44,212,190 | T | T | 0.240 | 0.271 | 1.27 ± 0.30 | 1.47 ± 0.33 | *EXT2* |
| rs1113132 | 11 | 44,209,979 | C | C | 0.237 | 0.267 | 1.15 ± 0.27 | 1.36 ± 0.31 | *EXT2* |

# Problemas actuales

- Participar en el diseño

*"To call in the statistician after the experiment is done may be no more than asking him to perform a post-mortem examination: he may be able to say what the experiment died of."*

*Ronald Fisher (1890-1962)*

# Problemas actuales

- Informar parcialmente de los valores de p:

~~p < 0,05~~

~~p: NS~~

p = 0,047 p = 0,003

p = 0,053 p = 0,648

## Problemas actuales

- Confundir significación estadística con significación clínica.

**Descenso en la TA: 20 mmHg**

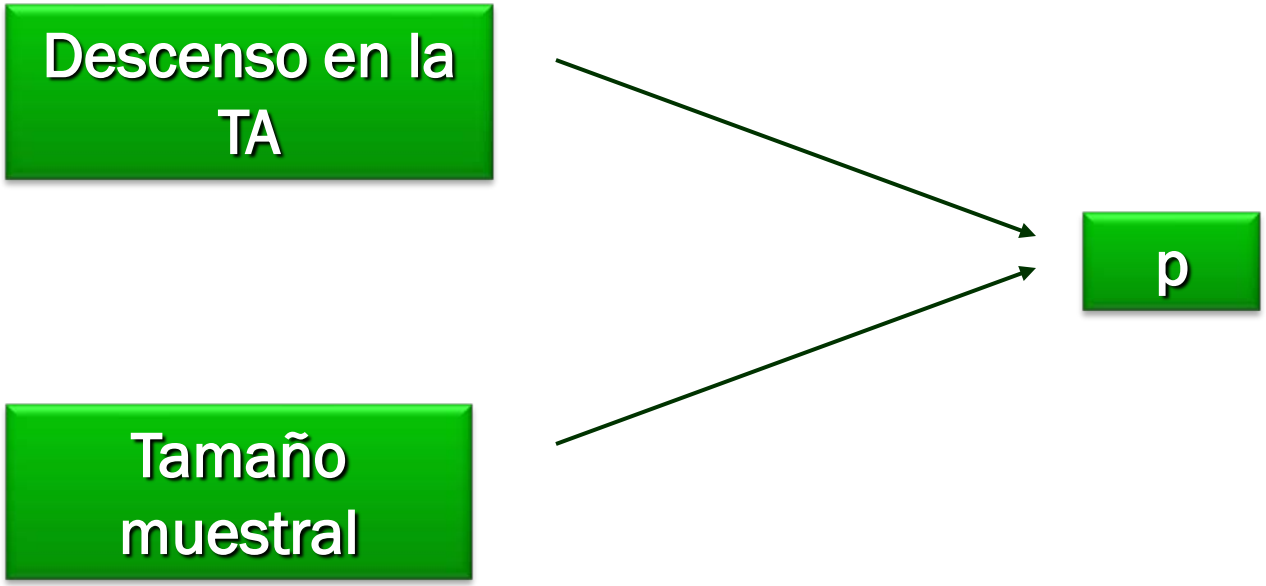
**p = 0,065**

**Descenso en la TA: 2 mmHg**

**p = 0,002**

# Problemas actuales

- Confundir el valor de p con la medida del efecto



# Problemas actuales

- No informar del número de sujetos en cada grupo.
- Informar de los porcentajes pero no del número absoluto.

**“50% de los varones mayores de 75 años tratados con placebo sufrieron un reinfarto.”**

“10 de los 20 varones mayores de 75 años tratados con placebo sufrieron un reinfarto.”

“2 de los 4 varones mayores de 75 años tratados con placebo sufrieron un reinfarto.”

# Problemas actuales

"Como tengo el manual del ecocardiógrafo puedo hacer cardiología."

"Como tengo el manual del SPSS puedo hacer estadística."

# Problemas actuales

- Utilizar varias mediciones del mismo paciente como si fueran independientes.

**La mayoría de las técnicas estadísticas habituales requieren observaciones independientes**

# Problemas actuales

- Análisis de subgrupos

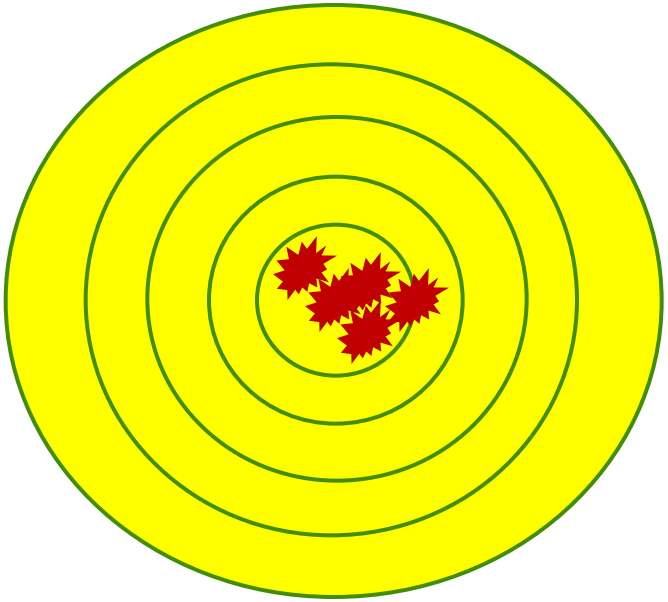
La aleatorización se diseñó para todo el grupo

La forma de identificar los subgrupos y de analizarlos debe estar definida en el diseño

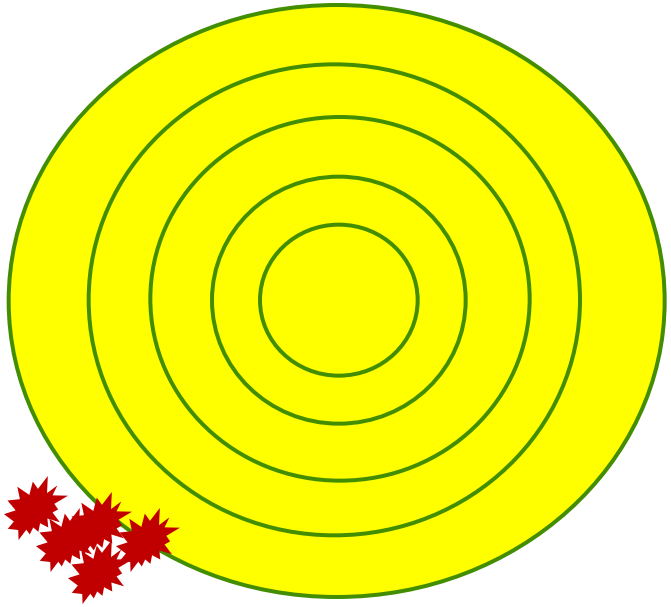
↓

Evitar los análisis post hoc

# Problemas actuales



# Problemas actuales



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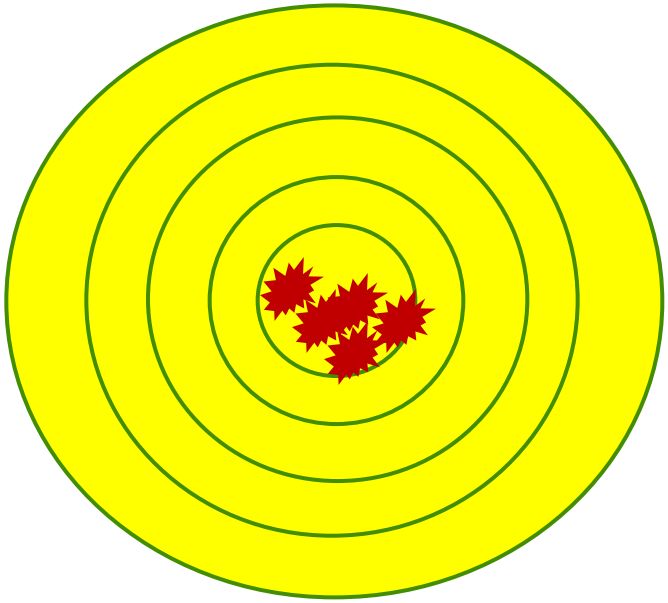
# Problemas actuales



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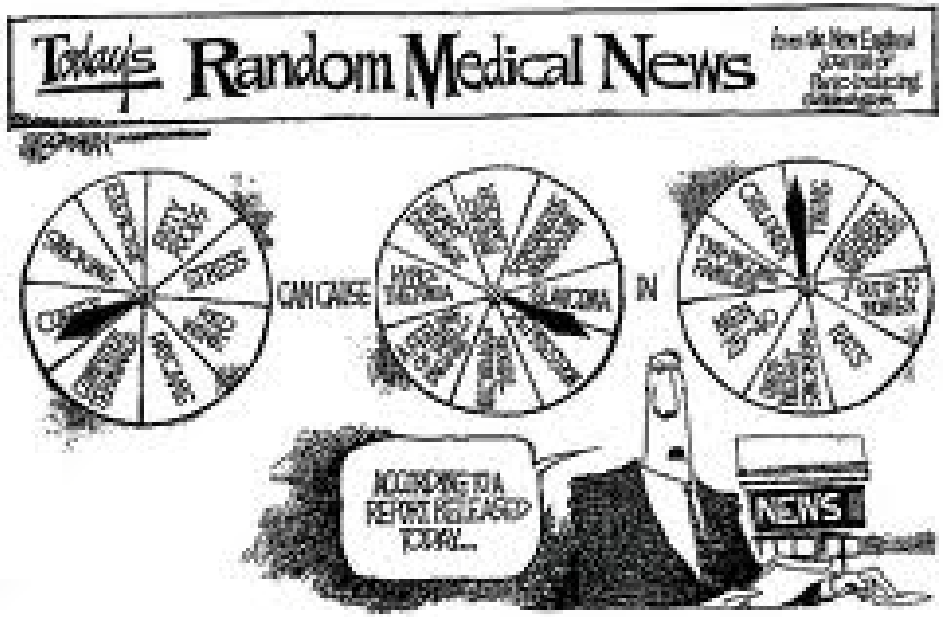
# Problemas actuales




One view of the value of epidemiology

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## Problemas actuales

# Fraud in clinical trials

## Detecting it and preventing it

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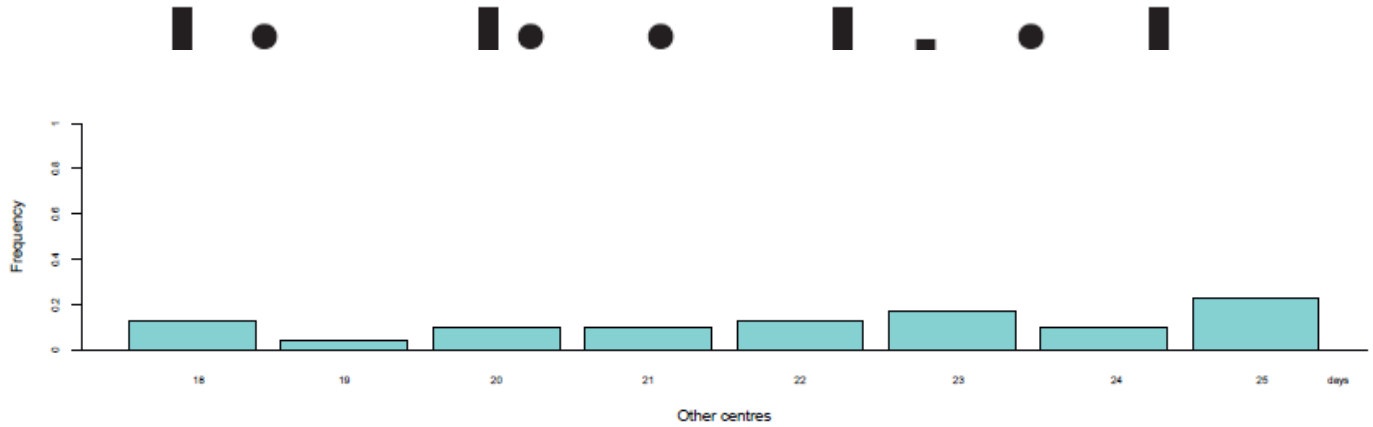
# Problemas actuales



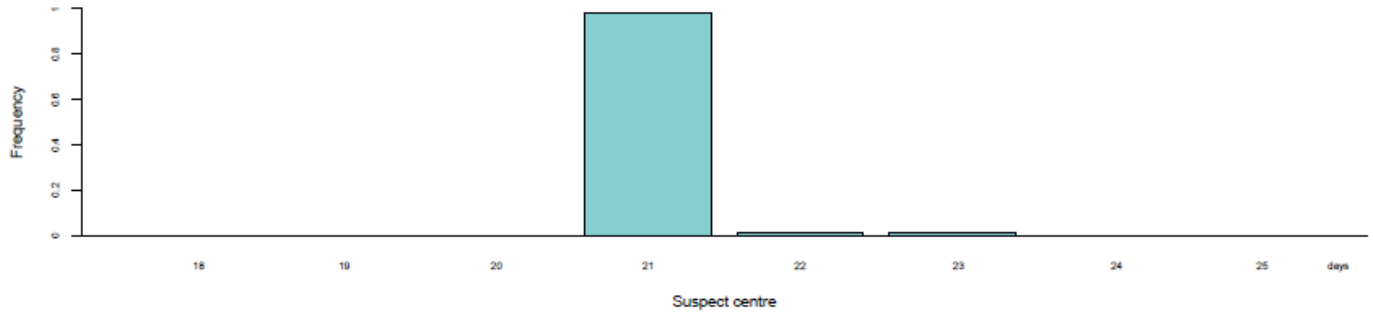




Figure 2. Near-perfect attendance on scheduled visit date raises concern regarding one study site. Based on Table IV data from Buyse *et al.*[3]

# Problemas actuales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# Análisis intermedios *(interim analyses)*

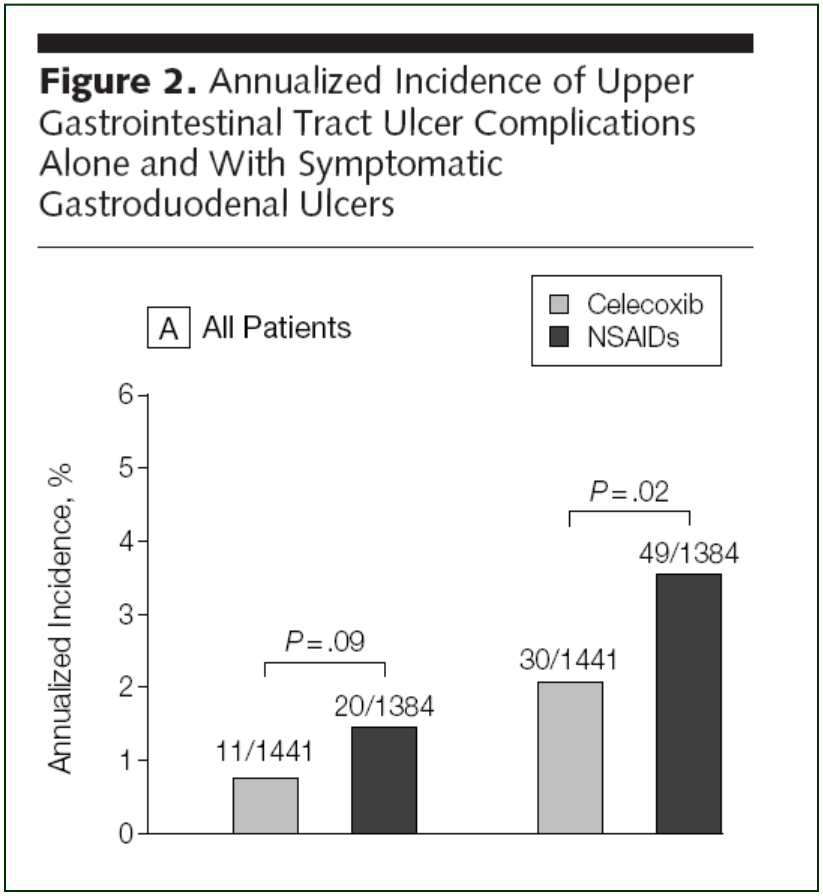
JAMA®

**Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study: A Randomized Controlled Trial**

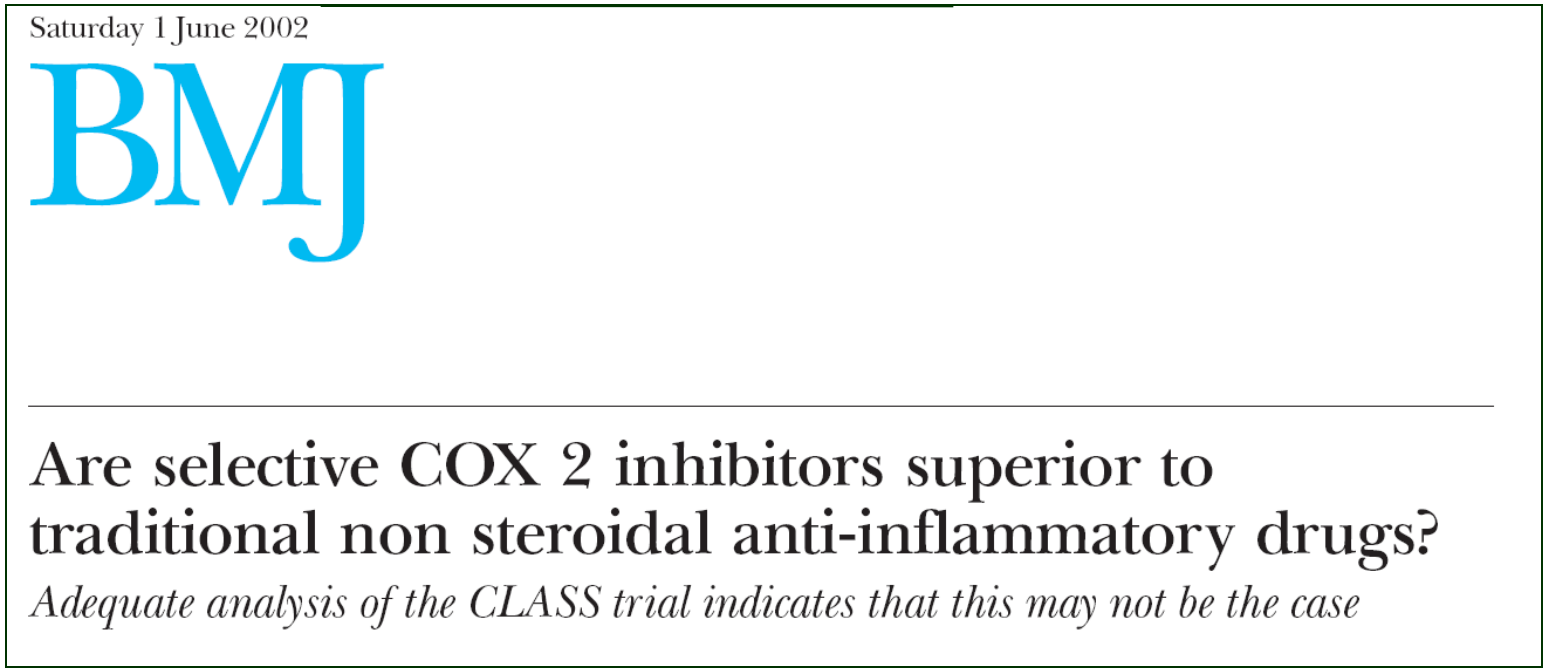
Fred E. Silverstein; Gerald Faich; Jay L. Goldstein; et al.

*JAMA*. 2000;284(10):1247-1255 (doi:10.1001/jama.284.10.1247)

# Análisis intermedios *(interim analyses)*



# Análisis intermedios *(interim analyses)*



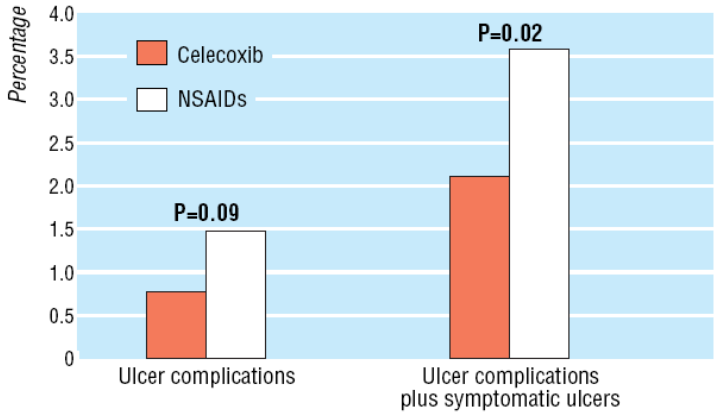
Saturday 1 June 2002

BMJ

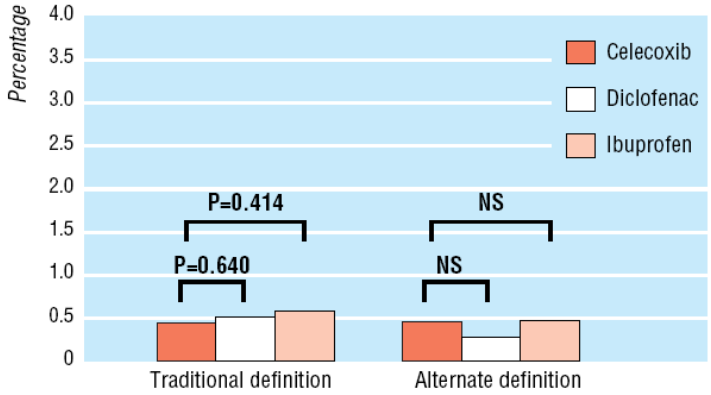
Are selective COX 2 inhibitors superior to traditional non steroidal anti-inflammatory drugs?

*Adequate analysis of the CLASS trial indicates that this may not be the case*

# Análisis intermedios *(interim analyses)*




*Annual rates extrapolated from 6 month follow up*




*Crude rates of ulcer complications based on entire follow up*

**Fig 1** Main results according to published report (top) and pre-specified protocol (bottom). Alternate definition of ulcer related complications, pre-specified by the FDA, included more stringent criteria to address serious gastrointestinal bleeding. P values are from log rank tests.

# Análisis intermedios *(interim analyses)*

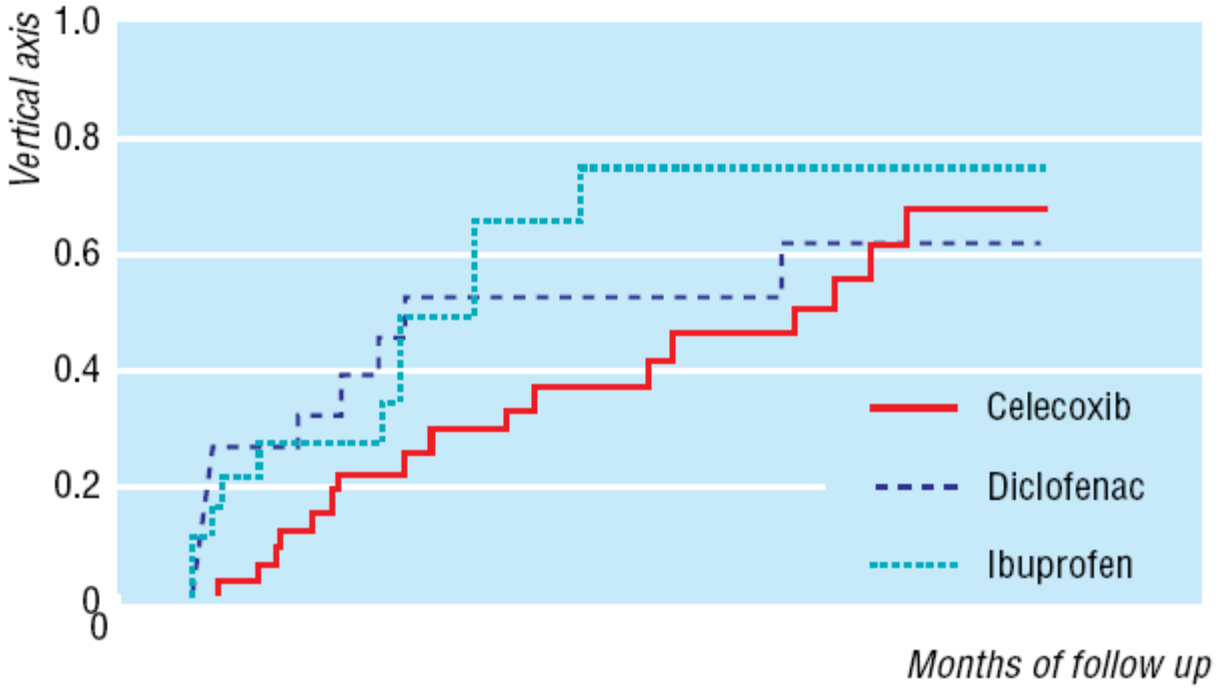


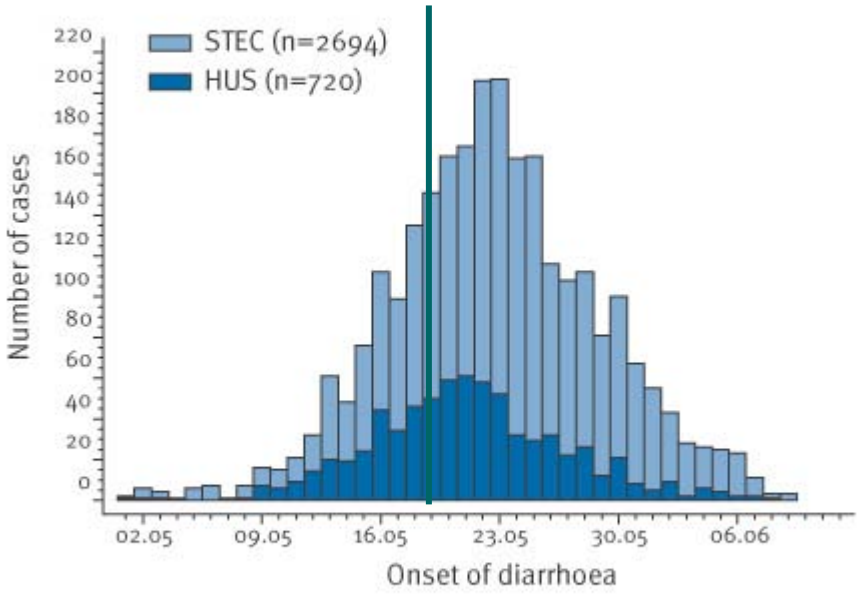

**Fig 2** Kaplan-Meier estimates for ulcer complications according to traditional definition. Results are truncated after 12 months, no ulcer complications occurred after this period. Adapted from Lu 2001.[7]

# Índice


- De las epidemias de cólera…
- Fases en el desarrollo de la epidemiología
- Tipos de estudio
- Herramientas de cálculo en la epidemiología actual
- ¿Para qué sirve la epidemiología?
- Nuestros problemas actuales
- … hasta la crisis de los pepinos

**FIGURE 2**

Reported STEC/VTEC and HUS cases, by date of onset of diarrhoea[a], Germany, May–June 2011 (n=2,694)




ED: Emergency department; HUS: haemolytic uraemic syndrome; STEC: Shiga toxin-producing *Escherichia coli*.

[a] Only cases with a notified date of onset since 1 May 2011.

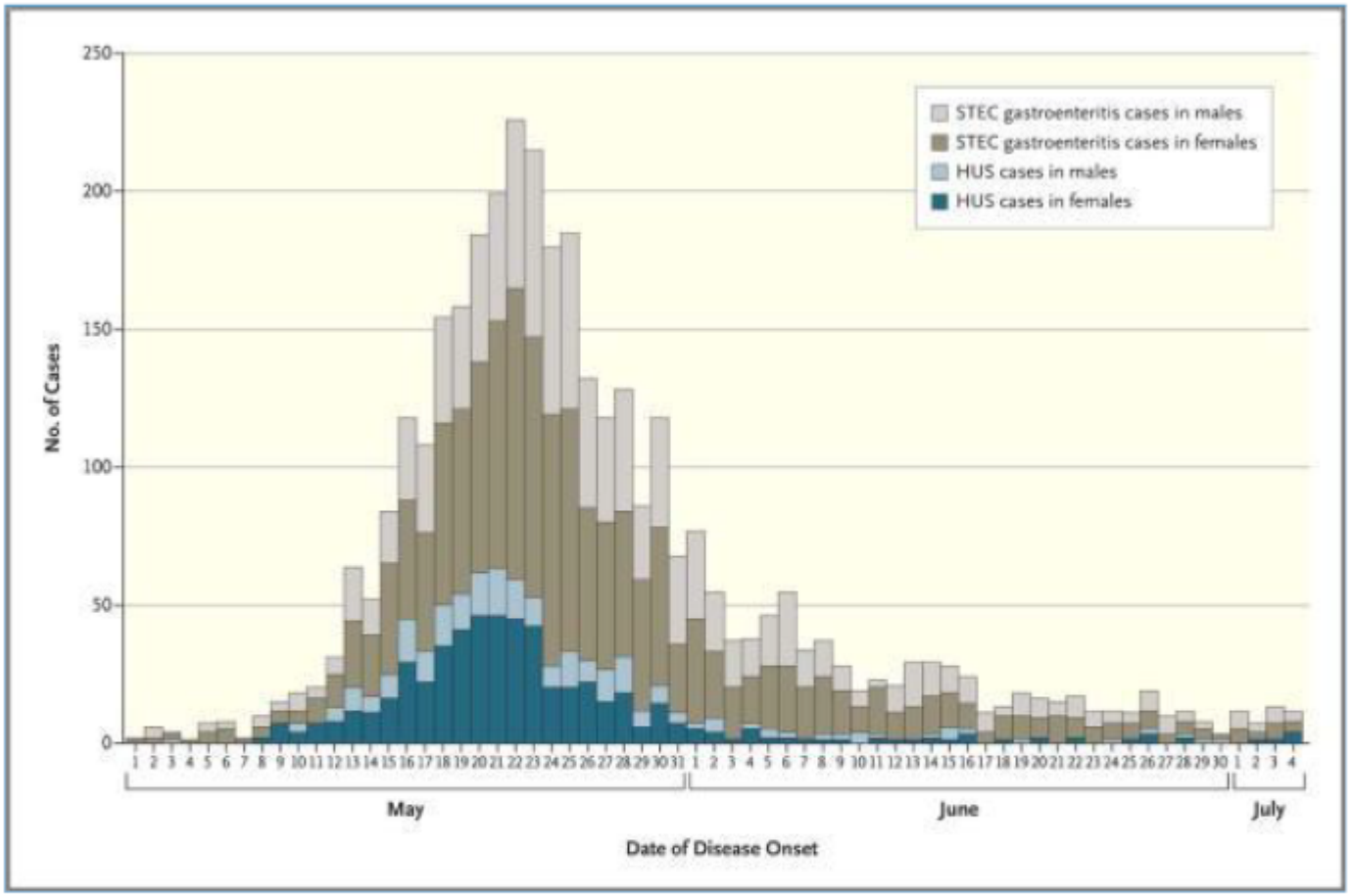
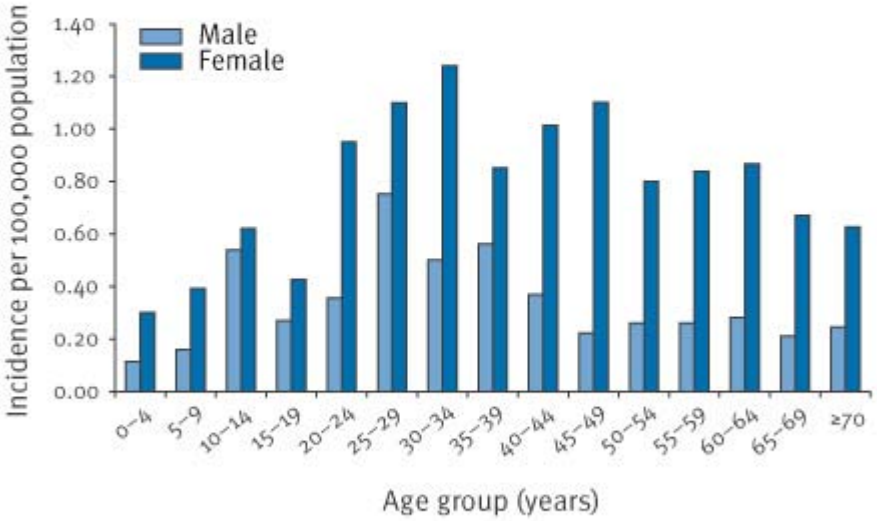



**Figure 2. Epidemiologic Curve of the Outbreak.** Shown are the numbers of cases of the hemolytic-uremic syndrome (HUS) and of Shiga-toxin-producing *Escherichia coli* (STEC) gastroenteritis, according to sex. Only cases with a known date of onset are included here — 802 of 845 cases of the hemolytic-uremic syndrome and 2700 of 2971 cases of Shiga-toxin-producing *E. coli* diarrhea.

**FIGURE 2**

Cumulative incidence of HUS cases notified since 1 May 2011, by age and sex, Germany (n=470)




HUS: haemolytic uraemic syndrome.
Data as of 31 May 2011, 3 pm.

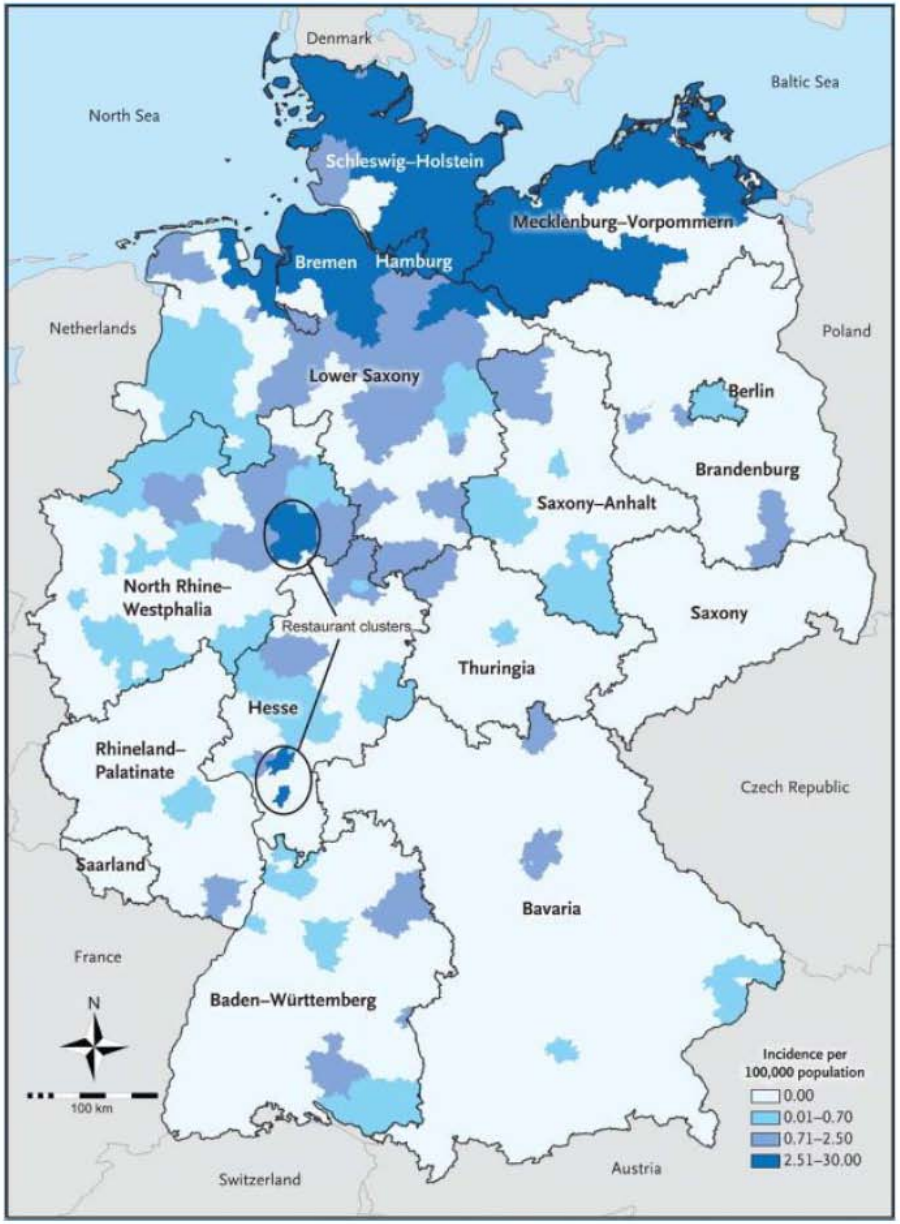



**Figure 1. Incidence of the Hemolytic-Uremic Syndrome According to County in Germany.** The incidence shown is per 100,000 population. A total of 845 cases were detected in this outbreak. Cases are attributed to a particular county if that county was the probable site of infection.

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# Casos acumulados

| País | SUH | No SUH | Total |
|---|---|---|---|
| Alemania | 810 | 2684 | 3494 |
| Austria | 1 | 3 | 4 |
| Dinamarca | 9 | 12 | 21 |
| España | 1 | 1 | 2 |
| Francia | 0 | 2 | 2 |
| Grecia | 0 | 1 | 1 |
| Holanda | 4 | 4 | 8 |
| Luxemburgo | 1 | 1 | 2 |
| Noruega | 0 | 1 | 1 |
| Polonia | 2 | 1 | 3 |
| R. Checa | 0 | 1 | 1 |
| Reino Unido | 3 | 3 | 6 |
| Suecia | 18 | 30 | 48 |

# Muertes acumuladas

| País | SUH | No SUH | Total |
|---|---|---|---|
| Alemania | 27 | 12 | 39 |
| Austria | 0 | 0 | 0 |
| Dinamarca | 0 | 0 | 0 |
| España | 0 | 0 | 0 |
| Francia | 0 | 0 | 0 |
| Grecia | 0 | 0 | 0 |
| Holanda | 0 | 0 | 0 |
| Luxemburgo | 0 | 0 | 0 |
| Noruega | 0 | 0 | 0 |
| Polonia | 0 | 0 | 0 |
| R. Checa | 0 | 0 | 0 |
| Reino Unido | 0 | 0 | 0 |
| Suecia | 1 | 0 | 1 |

- Estudio de casos y controles:
  - 25 casos
  - 81 controles emparejados por edad, sexo y residencia

Consumption of each of the named food items was reported by around 90% of the cases in comparison to around 60% of the controls, yielding odds ratios between around 4 and 7, all statistically significant. Nevertheless it is possible that another or an additional food item is the source of infection.

**Table 1. Vegetables or Fruits Evaluated in a Case–Control Study in the German Outbreak.***

| Food Item | Case Subjects Exposed | Control Subjects Exposed | Matched Odds Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *no./total no. (%)* | | | |
| Sprouts | 6/24 (25) | 7/80 (9) | 4.35 (1.05–18.0) | 0.04 |
| Cucumbers | 22/25 (88) | 52/79 (66) | 3.53 (0.96–12.9) | 0.06 |
| Apples | 22/24 (92) | 57/81 (70) | 3.91 (0.86–17.7) | 0.08 |
| Peppers | 16/24 (67) | 35/80 (44) | 2.66 (0.90–7.9) | 0.08 |
| Strawberries | 19/26 (73) | 43/81 (53) | 2.33 (0.90–6.0) | 0.08 |

* P>0.10 for raw onions, tomatoes, leaf salad, asparagus, carrots, and basil.

Table 1. Vegetables or Fruits Evaluated in a Case-Control Study in the German Outbreak.

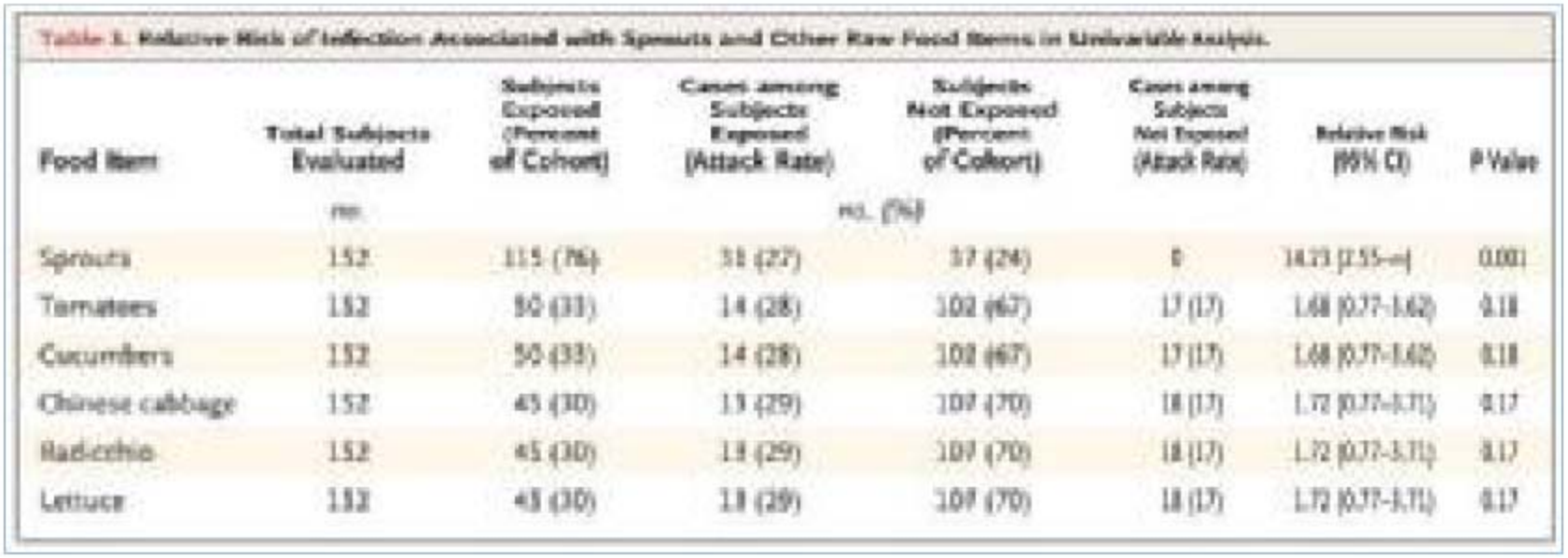


Table 3. Relative Risk of Infection Associated with Sprouts and Other Raw Food Items in Univariable Analysis.

| Food Item | Total Subjects Evaluated | Subjects Exposed (Percent of Cohort) | Cases among Subjects Exposed (Attack Rate) | Subjects Not Exposed (Percent of Cohort) | Cases among Subjects Not Exposed (Attack Rate) | Relative Risk (95% CI) | P Value |
|---|---|---|---|---|---|---|---|
| | no. | no. (%) | | | | | |
| Sprouts | 152 | 115 (76) | 31 (27) | 37 (24) | 0 | 14.23 [2.55–∞] | 0.001 |
| Tomatoes | 152 | 50 (33) | 14 (28) | 102 (67) | 17 (17) | 1.68 [0.77–3.62] | 0.18 |
| Cucumbers | 152 | 50 (33) | 14 (28) | 102 (67) | 17 (17) | 1.68 [0.77–3.62] | 0.18 |
| Chinese cabbage | 152 | 45 (30) | 13 (29) | 107 (70) | 18 (17) | 1.72 [0.77–3.71] | 0.17 |
| Radicchio | 152 | 45 (30) | 13 (29) | 107 (70) | 18 (17) | 1.72 [0.77–3.71] | 0.17 |
| Lettuce | 152 | 45 (30) | 13 (29) | 107 (70) | 18 (17) | 1.72 [0.77–3.71] | 0.17 |

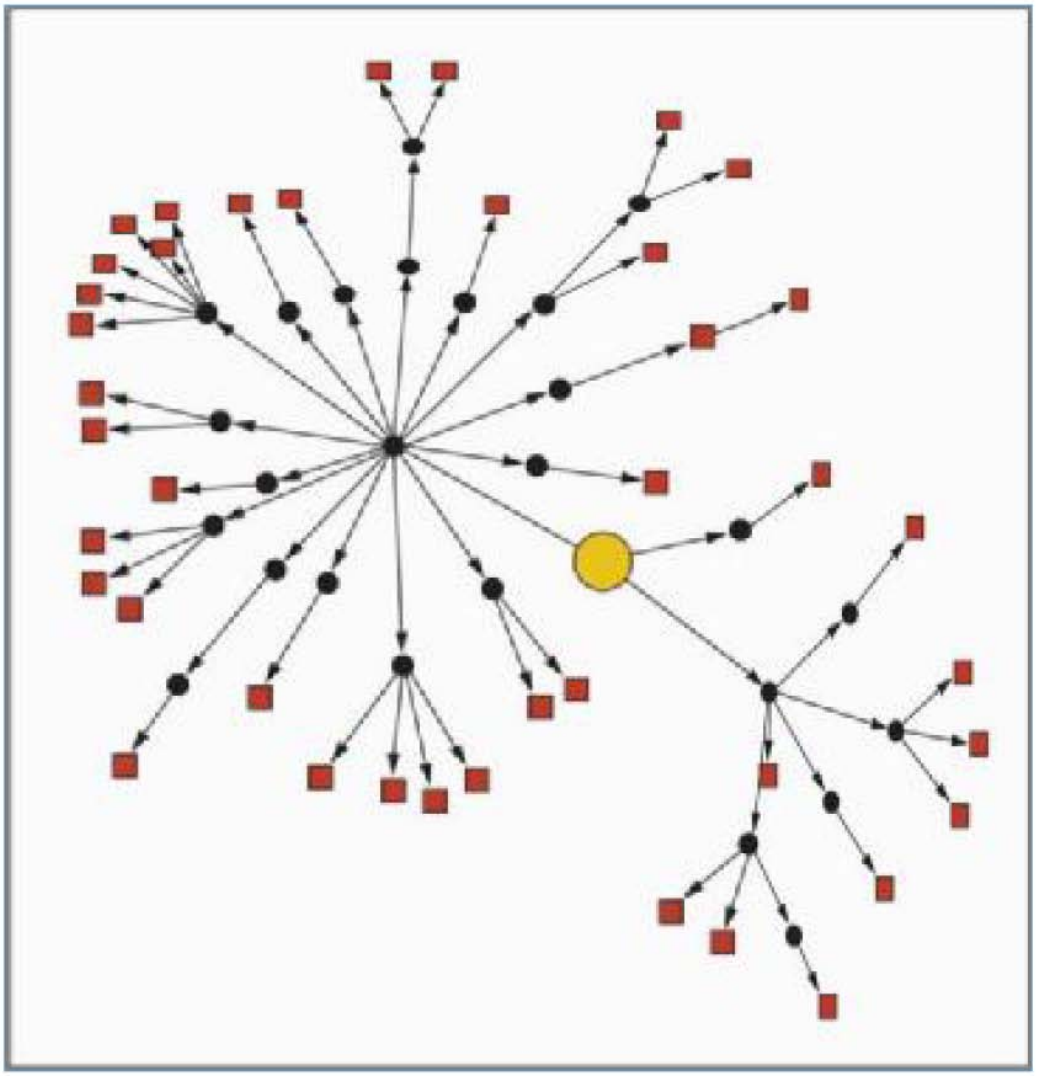


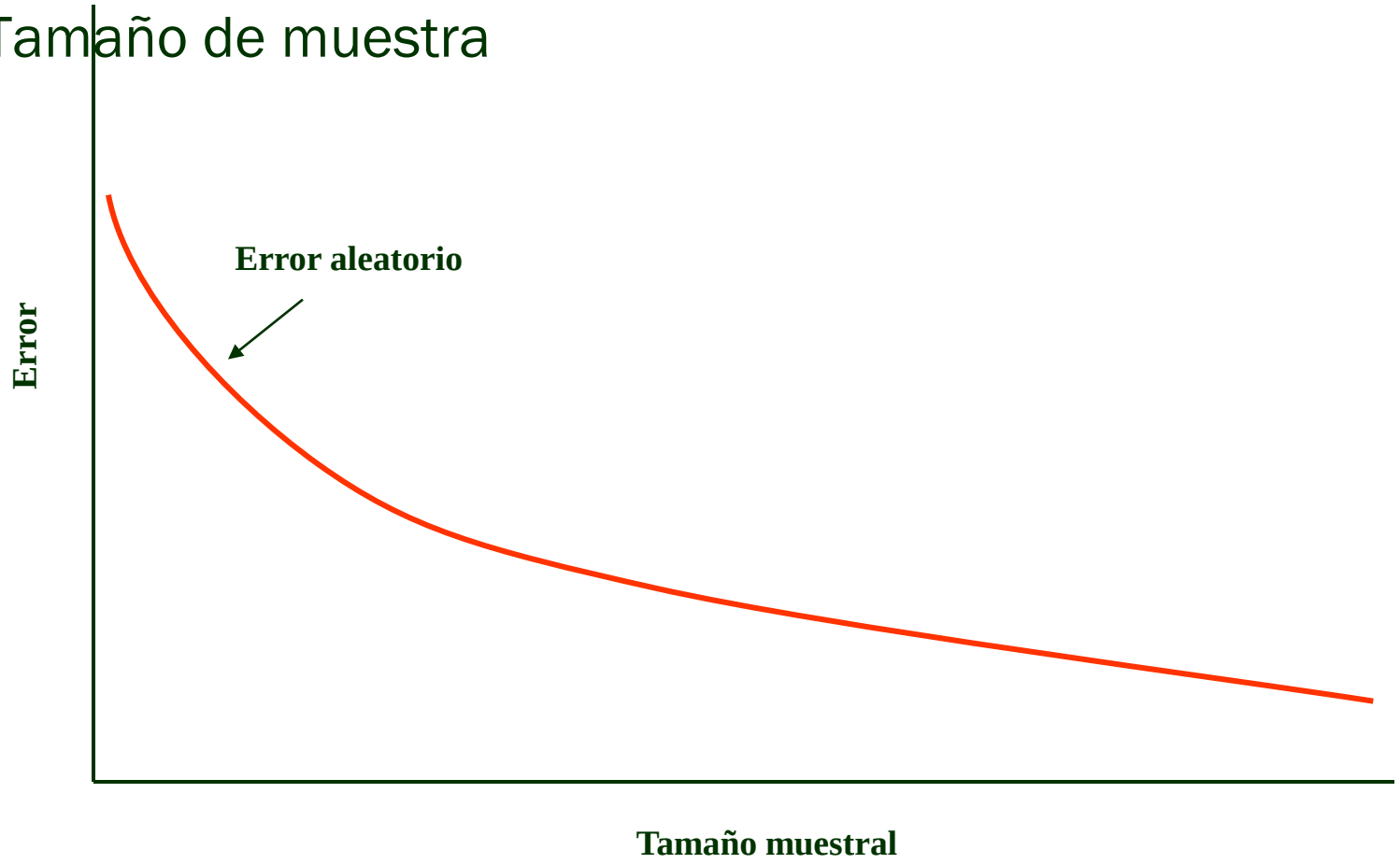
**Figure 2. Trading Network Leading to the German Outbreak.** The trading network for the contaminated sprouts led from producer A in Lower Saxony (yellow circle) to 26 sprout distributors (black dots) and 41 identified outbreak clusters (red squares), established by combined back and forward tracing.

# Posibles fuentes de error

- Tamaño de muestra
- Sesgo de información
- Sesgo de confusión
- Sobrevalorar los resultados microbiológicos

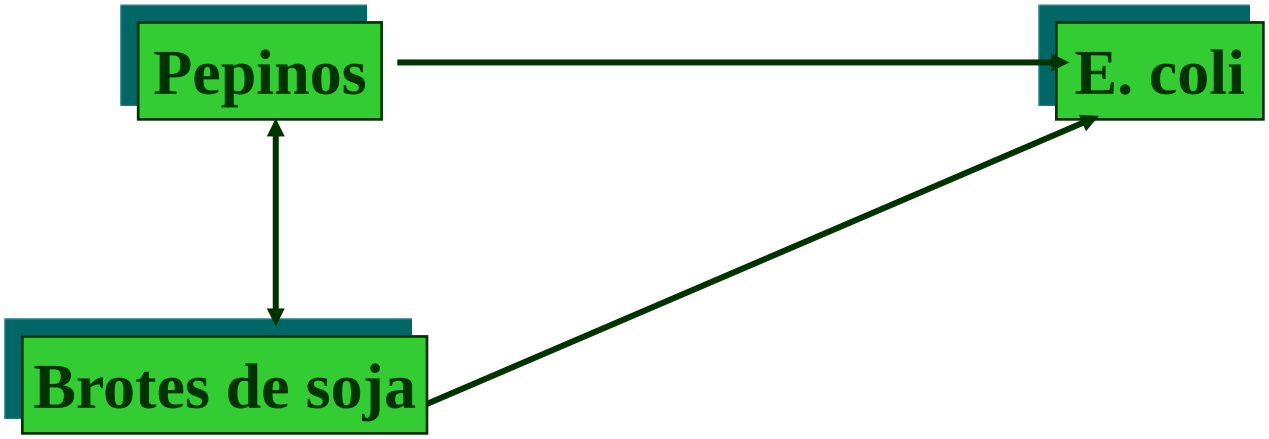
# Posibles fuentes de error

- Tamaño de muestra



# Posibles fuentes de error

- Sesgo de confusión



# Posibles fuentes de error

- Sobrevalorar los resultados microbiológicos:
  - Contaminación cruzada
  - Lotes contaminados / no contaminados

  - Presencia de E. coli ≠ fuente de transmisión

**Table 1. Vegetables or Fruits Evaluated in a Case–Control Study in the German Outbreak.***

| Food Item | Case Subjects Exposed | Control Subjects Exposed | Matched Odds Ratio (95% CI) | P Value |
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* P>0.10 for raw onions, tomatoes, leaf salad, asparagus, carrots, and basil.

Table 1. Vegetables or Fruits Evaluated in a Case-Control Study in the German Outbreak.

# Sesgo de información

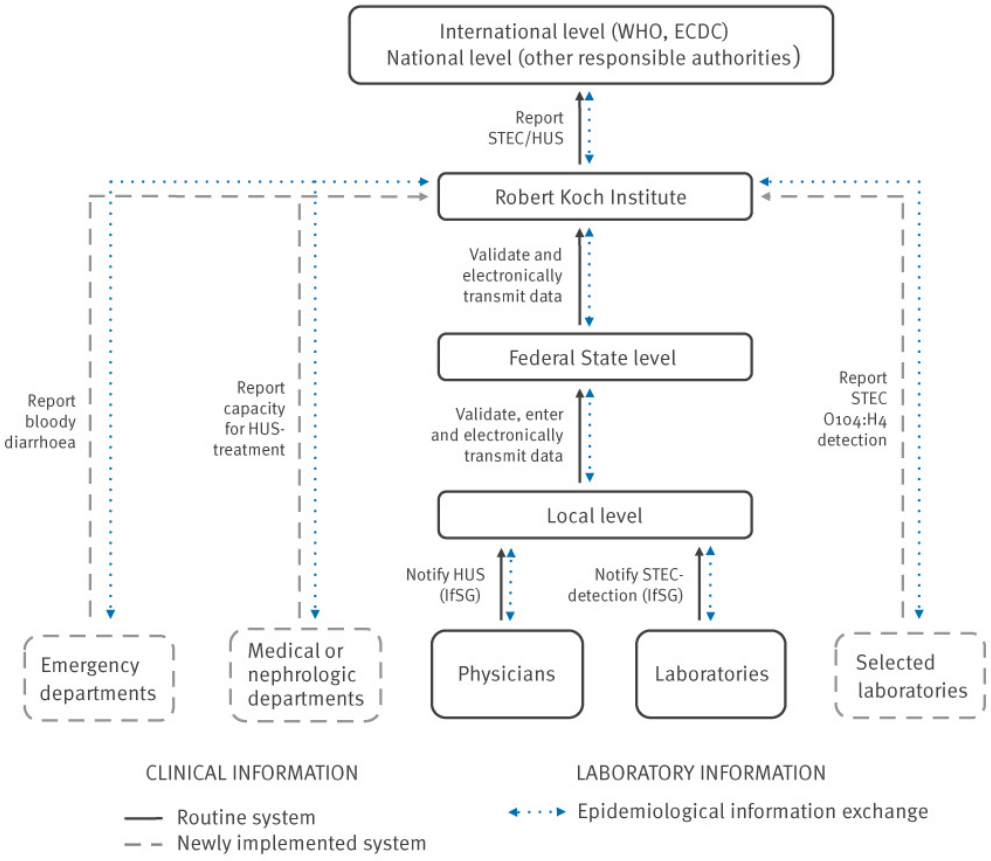
- Se reinterrogó sobre el consumo de brotes:
  - Varios casos cambiaron su información
  - Ningún control cambió

- GIGO (Garbage in, garbage out)

# Retraso en la identificación del brote

**FIGURE 1**

Data and information flow to and from the Robert Koch Institute during the period of enhanced surveillance, STEC/HUS outbreak, Germany, spring 2011




ECDC: European Centre for Disease Prevention and Control; HUS: haemolytic uraemic syndrome; IfSG: German Protection against Infection Act; STEC: Shiga toxin-producing Escherichia coli; WHO: World Health Organization.

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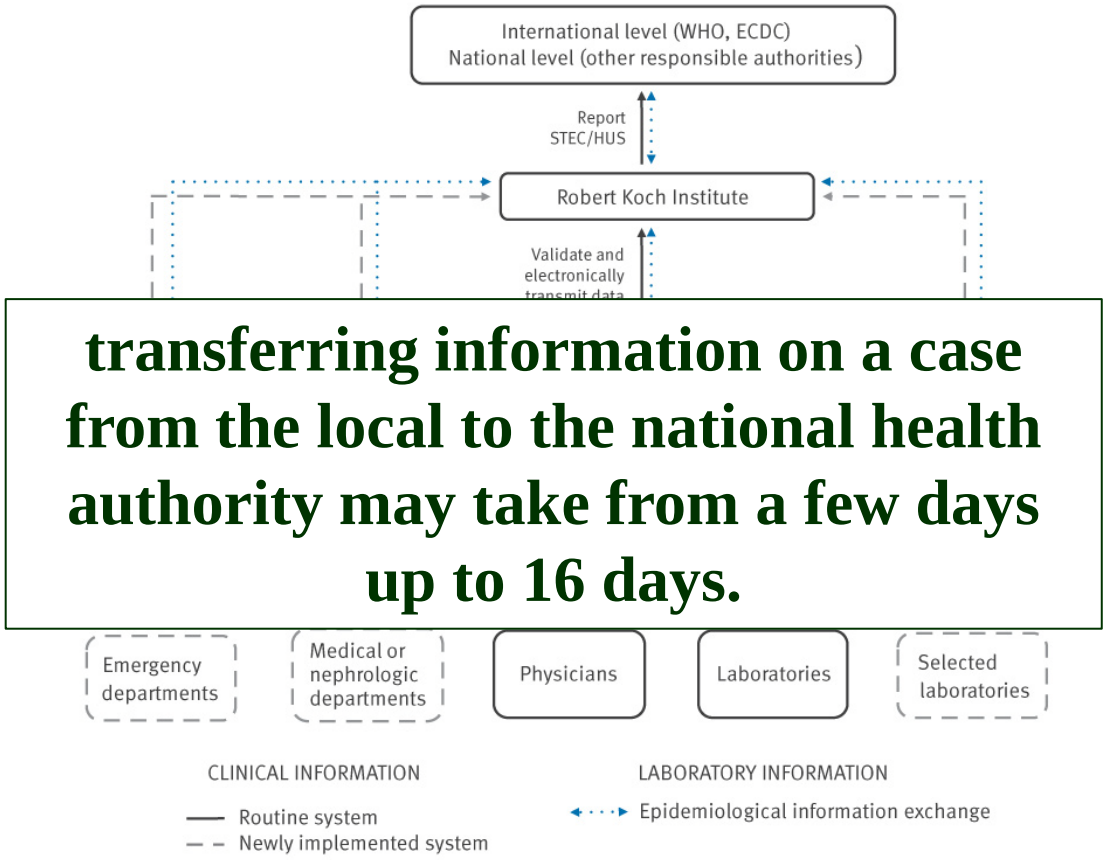
Epidemiología

# Retraso en la identificación del brote

**FIGURE 1**

Data and information flow to and from the Robert Koch Institute during the period of enhanced surveillance, STEC/HUS outbreak, Germany, spring 2011




**transferring information on a case from the local to the national health authority may take from a few days up to 16 days.**

ECDC: European Centre for Disease Prevention and Control; HUS: haemolytic uraemic syndrome; IfSG: German Protection against Infection Act; STEC: Shiga toxin-producing Escherichia coli; WHO: World Health Organization.

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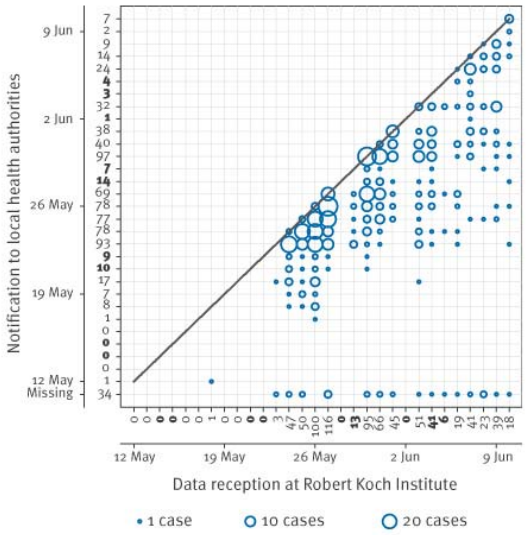
Epidemiología

# Retraso en la identificación del brote

**FIGURE 4**

Date of notification of HUS cases to local health authority in relation to date of reception at Robert Koch Institute, Germany, May–June 2011




HUS: haemolytic uraemic syndrome; PH: public holiday; STEC: Shiga toxin-producing *Escherichia coli*; WE: weekend.

Weekends and public holidays in bold; the x- and y-axis additionally show the number of reports received.

The size of the circle is equivalent to the number of cases (examples for 1, 10 and 20 cases shown in the legend).

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# Resumen

*"The statistician, however mathematical, has no magic spell which frees Dame Nature to treat him differently from other men. She always answers truthfully the question you ask her, not the question you meant to ask but the one you did ask."*

*Major Greenwood*

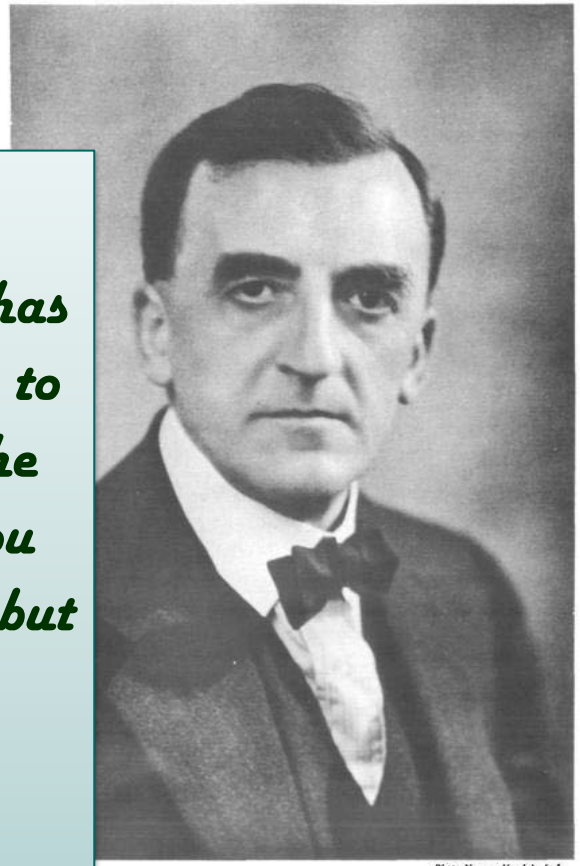
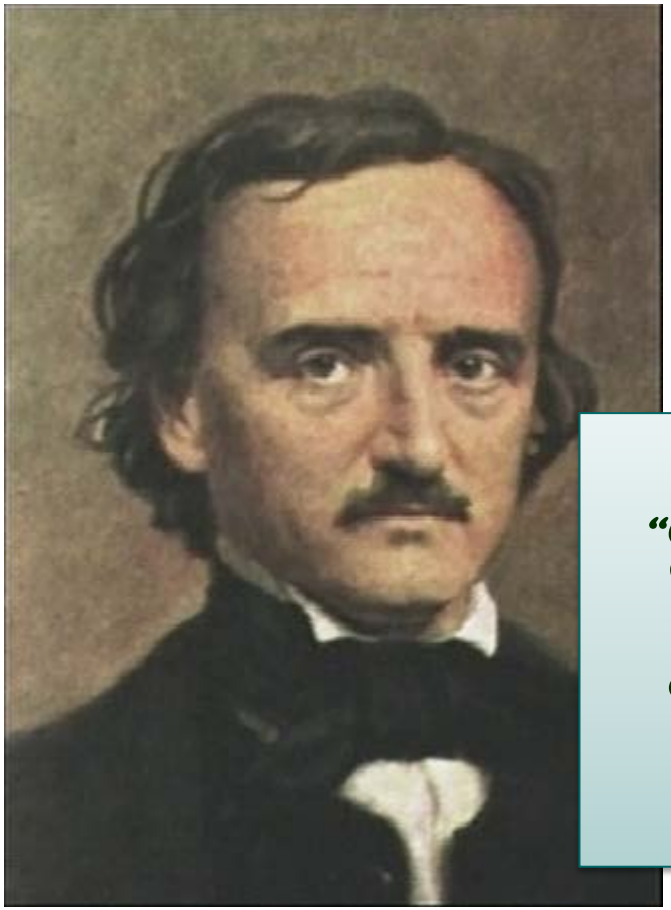


Photo Nowma Vandyk, Ltd.

MAJOR GREENWOOD
1880–1949

# Resumen



*"Yet to calculate is not in itself to analyze."*

*Edgar Allan Poe. The Murders in the Rue Morgue*

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- Death by water: John Snow and cholera in the XIXth century (Stephanie J. Snow)

http://www.lmi.org.uk/Data/10/Docs/11/11Snow.pdf

- John Snow: a historical giant in epidemiology (UCLA)

http://www.ph.ucla.edu/epi/snow.html

- Framingham Heart Study

http://www.framinghamheartstudy.org/risk/index.html

- MCC-Spain (Multi Caso Control – Spain)

http://mccspain.org/?q=es

- Proyecto SUN

http://www.unav.es/departamento/preventiva/sun

- Estudio PREDIMED

http://predimed.onmedic.net/