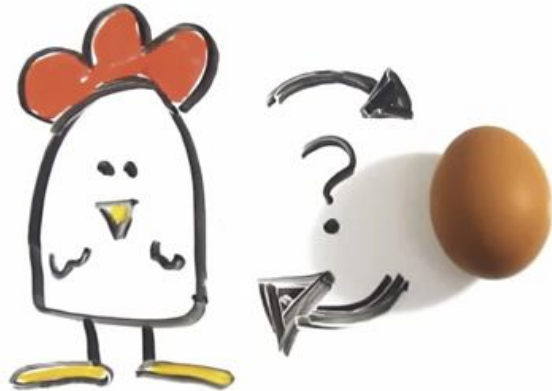


IA & SHS

Séance 4

"THE CHICKEN -OR- THE CHICKEN EGG"



“As a human being, you are already innately familiar with causal inference’s fundamental concepts.

Through sheer existence, you know what a causal effect is, understand the difference between association and causation, and you have used this knowledge consistently throughout your life.”

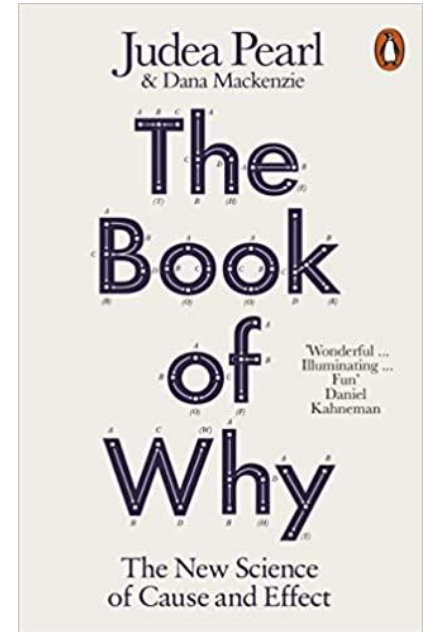
Miguel Hernan, Causal inference, What if?



“[...] falsely believing that the answers to all scientific questions reside in the data, to be unveiled through clever data-mining tricks. Much of this data-centric history still haunts us today. We live in an era that presumes Big Data to be the solution to all our problems.

Courses in “data science” are proliferating in our universities, and jobs for “data scientists” are lucrative in the companies that participate in the “data economy.” But I hope with this book to convince you that data are profoundly dumb.”

Judea Pearl, The Book of Why: The New Science of Cause and Effect



Cause ou effet? Au-delà de la corrélation

Causalité

- Très facile de faire des erreurs;
- Quelles sont les hypothèses ?

→ Posez vous les bonnes questions. Rechercher un “effet” est rarement clair.

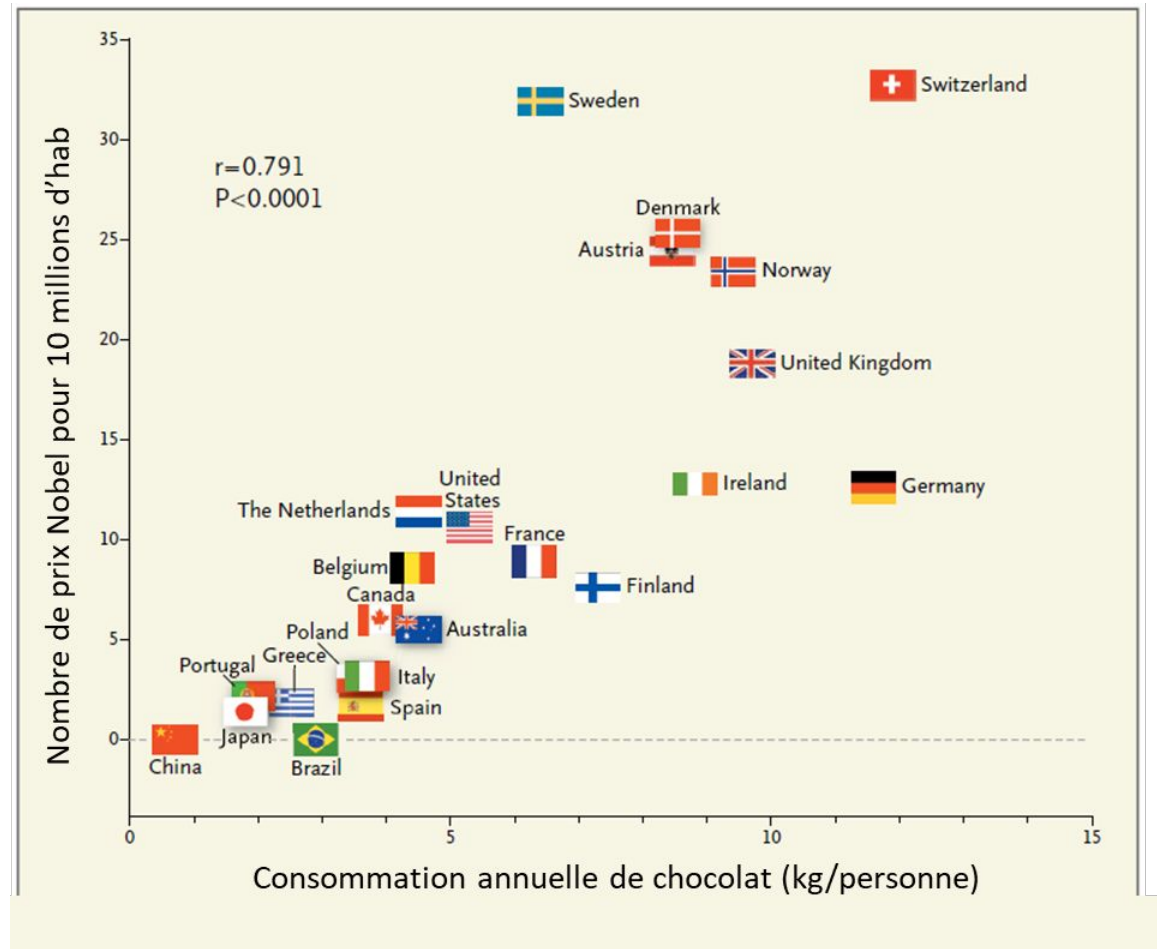
→  En pratique, vous trouverez toujours quelque chose à dire sur des données

Machine-Learning

- Possibilité de tester (ex. cross-validation)

But du cours

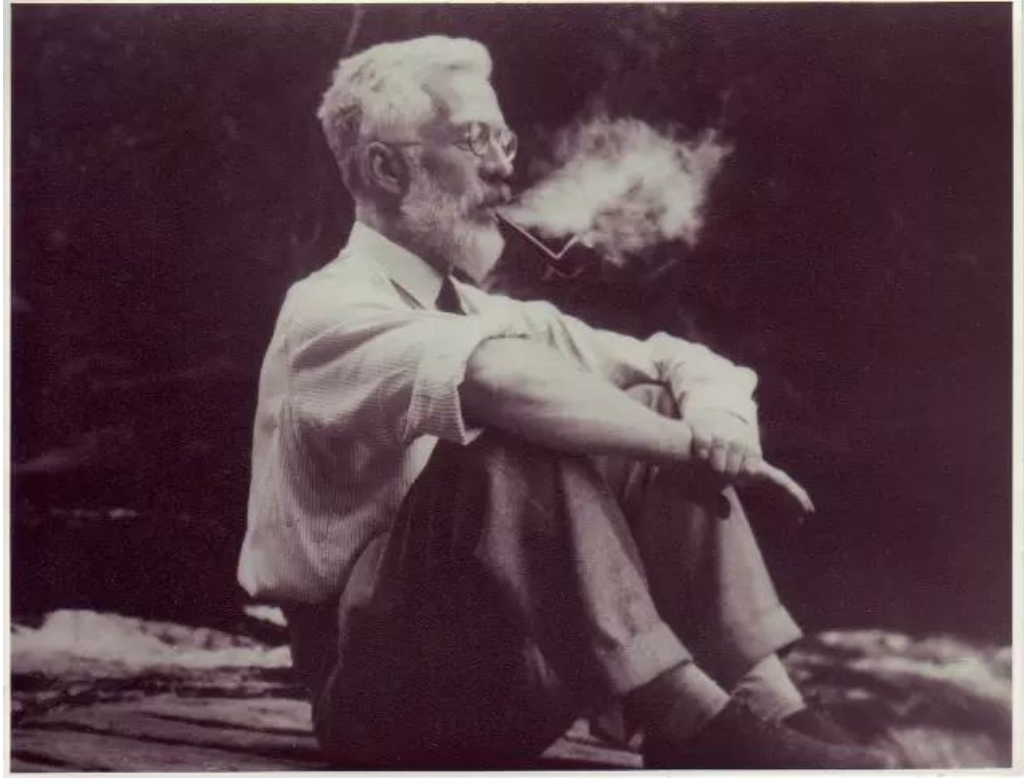
1. Apprendre à formuler les hypothèses qui permettent de conclure à un effet dit causal
 - a. Différencier association de causalité
 - b. Analyse d'études randomisées
 - c. Formalisation dans le formalisme des "potential outcomes" de Neyman
2. Estimer un effet causal à partir de données observationnelles (Matching)
3. Application



Source: <http://journal-decoder.fr/> d'après Messerli, 2012.



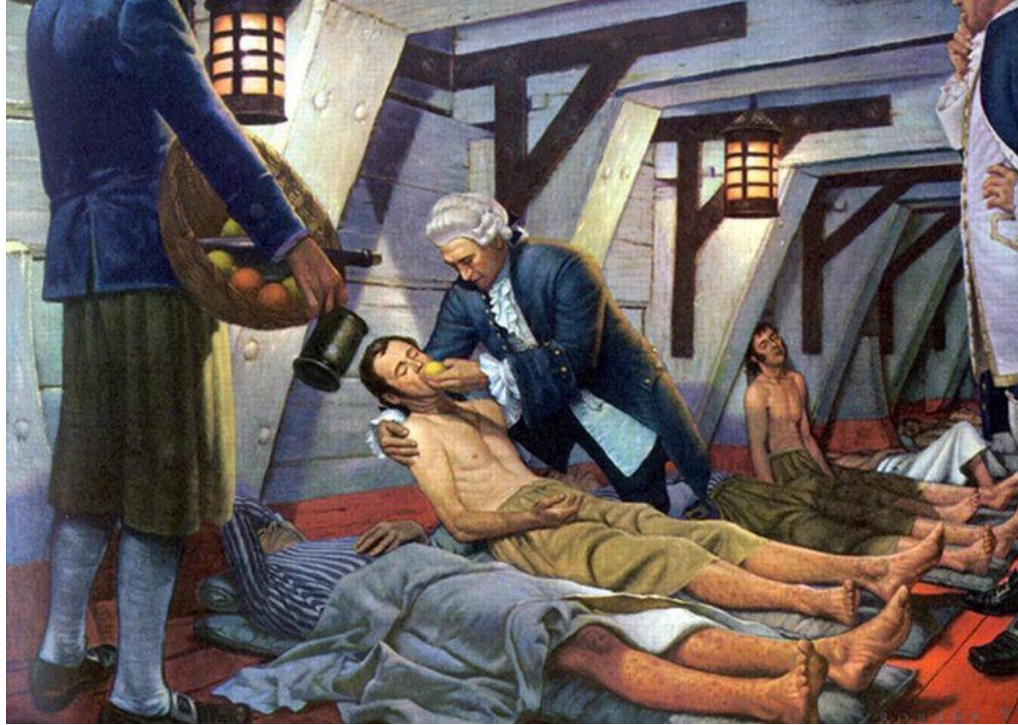
Source: Exemple tiré de “The book of Why”, J. Pearl - Image: Current Biology, Shimmura et al.



Source: Ronald A. Fisher

Connaissez-vous un cas où une association est causale?

Connaissez-vous un cas où une association est causale?



Source: Institute of naval medicine via BBC

No.	Drug Name	Active Ingredient	Approval Date	FDA-approved use on approval date*
37.	NexoBrid	anacaulase-bcdb	12/28/2022	To remove eschar in adults with deep partial thickness or full thickness thermal burns
36.	Briumvi	ublituximab-xiyy	12/28/2022	To treat relapsing forms of multiple sclerosis
35.	Xenoview	hyperpolarized Xe-129	12/23/2022	To evaluate pulmonary function and imaging
34.	Lunsumio	mosunetuzumab-axgb	12/22/2022	To treat adults with relapsed or refractory follicular lymphoma, a type of non-Hodgkin lymphoma
33.	Sunlenca	lenacapavir	12/22/2022	To treat adults with HIV whose HIV infections cannot be successfully treated with other available treatments due to resistance, intolerance, or safety considerations Press Release

Source: Screenshot datant du mois de février 2023 du site de la FDA



Neyman proposed and studied randomized experiments in 1923.

Furthermore, his paper "On the Two Different Aspects of the Representative Method: The Method of Stratified Sampling and the Method of Purposive Selection", given at the Royal Statistical Society on 19 June 1934, was the groundbreaking event leading to modern scientific sampling.

He introduced the confidence interval in his paper in 1937.

Another noted contribution is the Neyman–Pearson lemma, the basis of hypothesis testing.



Données observationnelles

Recent FDA Approval Shows the Value of RWE

➡ The August 2021 approval of Prograf (tacrolimus, Astellas Pharma) in combination with other immunosuppressant drugs for the prevention of organ rejection in adult and pediatric patients receiving lung transplantation was important not only because it was the first approval of a drug to prevent lung transplant rejection, but because it demonstrated how “fit-for-purpose” RWD/RWE could be effectively used to meet FDA requirements.⁷

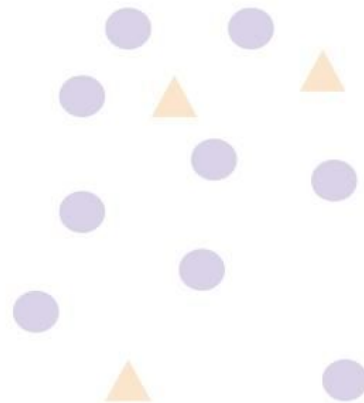
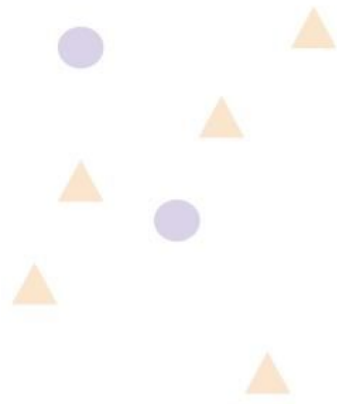
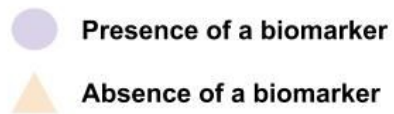
RWD and RWE used to support the approval of a drug candidate must meet specific FDA requirements, particularly legal and scientific evidentiary standards. In the case of Prograf, a non-interventional study was conducted using RWD from the U.S. Scientific Registry of Transplant Recipients for all lung transplants in the United States.⁷ Additional mortality data was collected from the Social Security Administration’s Death Master File. The data clearly showed that lung transplant patients receiving Prograf experienced dramatically improved outcomes compared with patients that received no or minimal immunosuppressive therapy, reducing concerns of bias in the data. These results were supported by clinical data obtained in randomized controlled trials of Prograf used in other solid organ transplant settings.

The approval of Prograf provides a good example of the successful application of RWD/RWE to support regulatory decision making.⁷



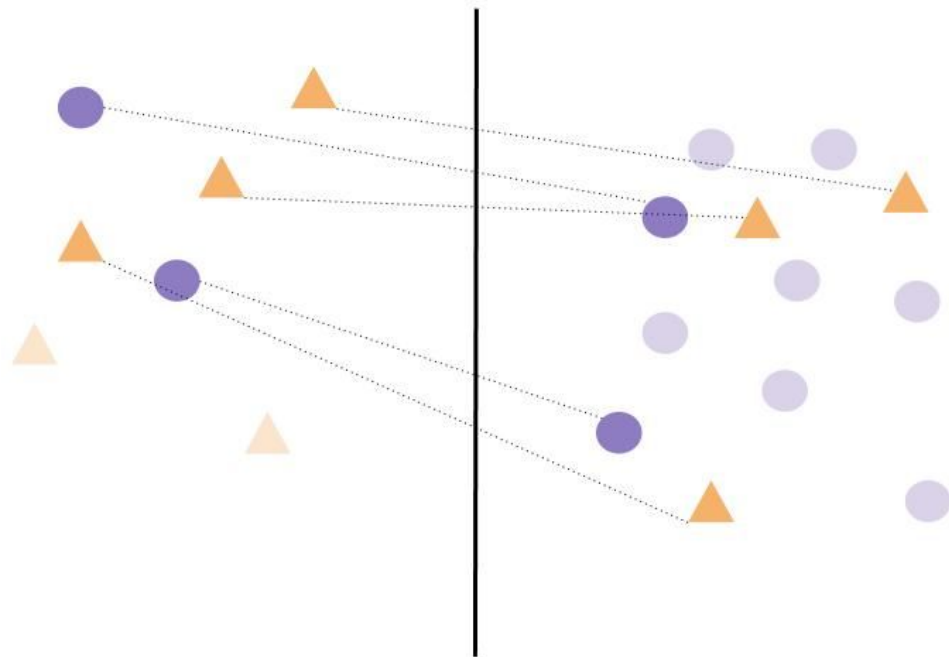
Treated



Control



Treated



Control



-  Presence of a biomarker
-  Absence of a biomarker

Quelles hypothèses pour que l'inférence soit correcte?

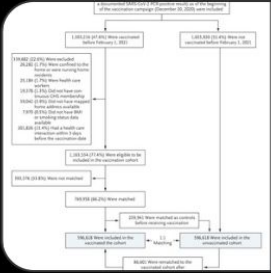
These methods were used very recently

 **Miguel Hernán**  @_MiguelHernan · Feb 24, 2021

1/
We've just confirmed the effectiveness of the Pfizer-BioNTech vaccine outside of randomized trials.

Details [@NEJM: nejm.org/doi/full/10.10...](https://www.nejm.org/doi/full/10.1056/NEJMoa2102454)

Yes, great news, but let's talk about methodological issues that arise when using [#observational](#) data to estimate vaccine effectiveness.



nejm.org
BNT162b2 mRNA Covid-19 Vaccine in a Nationwi...
Original Article from The New England Journal of Medicine — BNT162b2 mRNA Covid-19 Vaccine i...

Conclusions

- Exposition de la question
- Introduction au formalisme des “potential outcomes”
- Présentation de l’une des méthodes pour estimer un effet à partir de données non-randomisées (i.e. observationnelles)
- D’autres méthodes existent
- Dans ce cours nous n’avons pas vu comment inférer un graphique

Hands-on!

