Enseigner et illustrer l'approche bayésienne avec la COVID-19

Retour d'expérience

Boris Hejblum

Contexte

STA305 / INITBAYES / Intro Bayes Med

Chaque année:

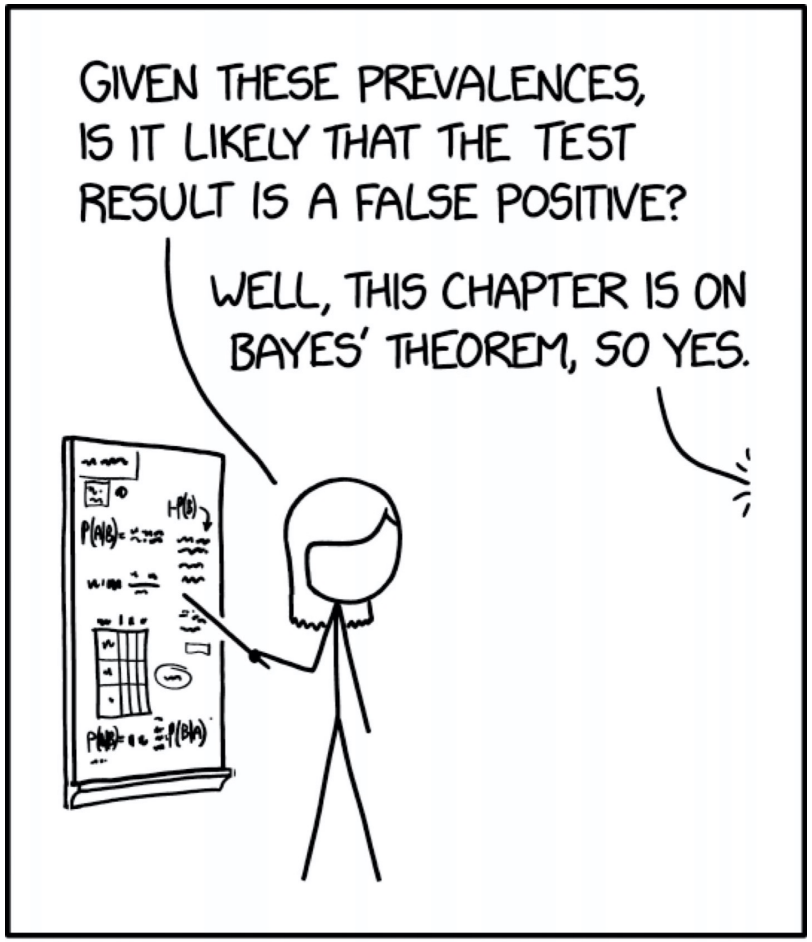
- M2 Biostatistique — ISPED (STA305)

- Cours doctoral — École d'été de l'ISPED / EUR *Digital Public Health*

- *Graduate class — University of Copenhaguen (Bayesian methods for biomedical research)*

Théorème de Bayes et pandémie

L’exemple de la maladie « rare » pour les probabilités conditionnelles



Source : xkcd

L’exemple de la maladie « rare » pour les probabilités conditionnelles

- *Seeing theory*

  Brown University

https://seeing-theory.brown.edu/bayesian-inference/index.html

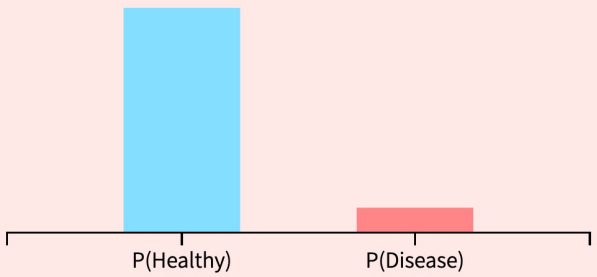
Chapter 5: Bayesian Inference

Bayes' Theorem

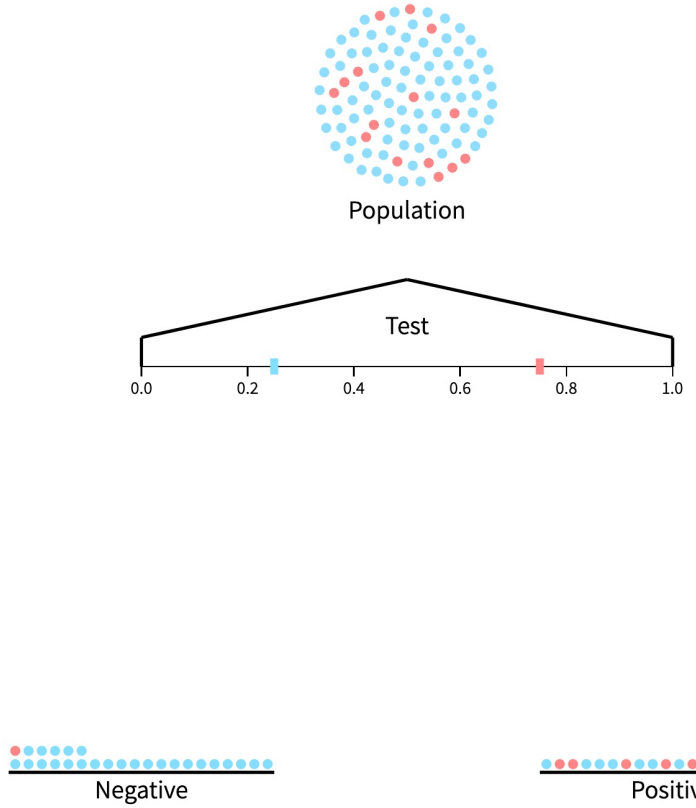
Suppose that on your most recent visit to the doctor's office, you decide to get tested for a rare disease. If you are unlucky enough to receive a positive result, the logical next question is, "Given the test result, what is the probability that I actually have this disease?" (Medical tests are, after all, not perfectly accurate.) Bayes' Theorem tells us exactly how to compute this probability:

$$P(\text{Disease}|+) = \frac{P(+|\text{Disease})P(\text{Disease})}{P(+)}$$

As the equation indicates, the *posterior* probability of having the disease given that the test was positive depends on the *prior* probability of the disease $P(\text{Disease})$. Think of this as the incidence of the disease in the general population. Set this probability by dragging the bars below.



The posterior probability also depends on the test accuracy: How often does the test correctly report a negative result for a healthy patient, and how often does it report a positive result for someone with the disease? Determine these two distributions below.



Probabilités conditionnelle revisitées avec les tests antigéniques

- **Incidence** de l'infection en France la semaine du 16 novembre[1] : $0,151\%$
- Propriétés du test antigénique[2] :
  - Sensibilité : 71%
  - Spécificité : 98%

Avec un test positif, quelle est la probabilité d'avoir réellement la COVID-19 ?

$$\Pr(M=+)=0.151 \quad \Pr(T=+|M=+)=0.71 \quad \Pr(T=-|M=-)=0.98$$

$$\begin{aligned}
\Pr(M=+|T=+) &= \frac{\Pr(T=+|M=+)\Pr(M=+)}{\Pr(T=+)} \\
&= \frac{\Pr(T=+|M=+)\Pr(M=+)}{\Pr(T=+|M=+)\Pr(M=+)+\Pr(T=+|M=-)\Pr(M=-)} \\
&= \frac{\Pr(T=+|M=+)\Pr(M=+)}{\Pr(T=+|M=+)\Pr(M=+)+(1-\Pr(T=-|M=-))(1-\Pr(M=+))} \\
&= 0.86
\end{aligned}$$

[1] Source : bulletin épidémiologique de Santé Publique France en semaine 47 2020

[2] Source : méta-analyse de la synthèse Haute Autorité de Santé du 8 Octobre 2020

Tests PCR : sensibilité et spécificité inconnues

Concise Research Report | Published: 03 June 2020

Interpreting COVID-19 Test Results: a Bayesian Approach

Chester B. Good MD, MPH ✉, Inmaculada Hernandez Pharm D, PhD & Kenneth Smith MD, MS

Journal of General Internal Medicine **35**, 2490–2491 (2020) | Cite this article

Good et al. J GEN INTERN MED 2020

Estimates for Post-Test Probability of Acute COVID-19 Infection for Simulated Patient Scenarios

Clinical Scenarios	Pre-test probability (%)	PCR assay sensitivity (%)	Post-test probability of acute COVID-19 infection	
			Positive test (%)	Negative test (%)
Patient 1: high pre-test proba-bility	70	70	100	41.2
		90	100	18.9
	90	70	100	73.0
		90	100	47.4
Patient 2: low pre-test probability	5	70	97.4	1.6
		90	97.9	0.5
	10	70	98.7	3.2
		90	99.0	1.1

Motivation pour comprendre l'approche bayésienne

Phase 3 du vaccin Pfizer-BioNTech

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Fernando P. Polack, M.D., Stephen J. Thomas, M.D., Nicholas Kitchin, M.D., Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Gonzalo Pérez Marc, M.D., Edson D. Moreira, M.D., Cristiano Zerbini, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., Satrajit Roychoudhury, Ph.D., Kenneth Koury, Ph.D., Ping Li, Ph.D., Warren V. Kalina, Ph.D., David Cooper, Ph.D., Robert W. Frenck, Jr., M.D., Laura L. Hammitt, M.D., Özlem Türeci, M.D., Haylene Nell, M.D., Axel Schaefer, M.D., Serhat Ünal, M.D., Dina B. Tresnan, D.V.M., Ph.D., Susan Mather, M.D., Philip R. Dormitzer, M.D., Ph.D., Uğur Şahin, M.D., Kathrin U. Jansen, Ph.D., and William C. Gruber, M.D., for the C4591001 Clinical Trial Group*

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.

† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.

‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

REMAP-CAP adaptive trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 22, 2021 VOL. 384 NO. 16

Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19

The REMAP-CAP Investigators*

lumab group, and 0 (interquartile range, –1 to 15) in the control group. The median adjusted cumulative odds ratios were 1.64 (95% credible interval, 1.25 to 2.14) for tocilizumab and 1.76 (95% credible interval, 1.17 to 2.91) for sarilumab as compared with control, yielding posterior probabilities of superiority to control of more than 99.9% and of 99.5%, respectively. An analysis of 90-day survival showed improved survival in the pooled interleukin-6 receptor antagonist groups, yielding a hazard ratio for the comparison with the control group of 1.61 (95% credible interval, 1.25 to 2.08) and a posterior probability of superiority of more than 99.9%. All secondary analyses supported efficacy of these interleukin-6 receptor antagonists.

ATTACC study from the REMAP-CAP trial

Design

CLINICAL TRIALS

Clinical Trials
1–10

DOI: 10.1177/1740774520943846
journals.sagepub.com/home/ctj
SAGE

Anti-Thrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC): Study design and methodology for an international, adaptive Bayesian randomized controlled trial

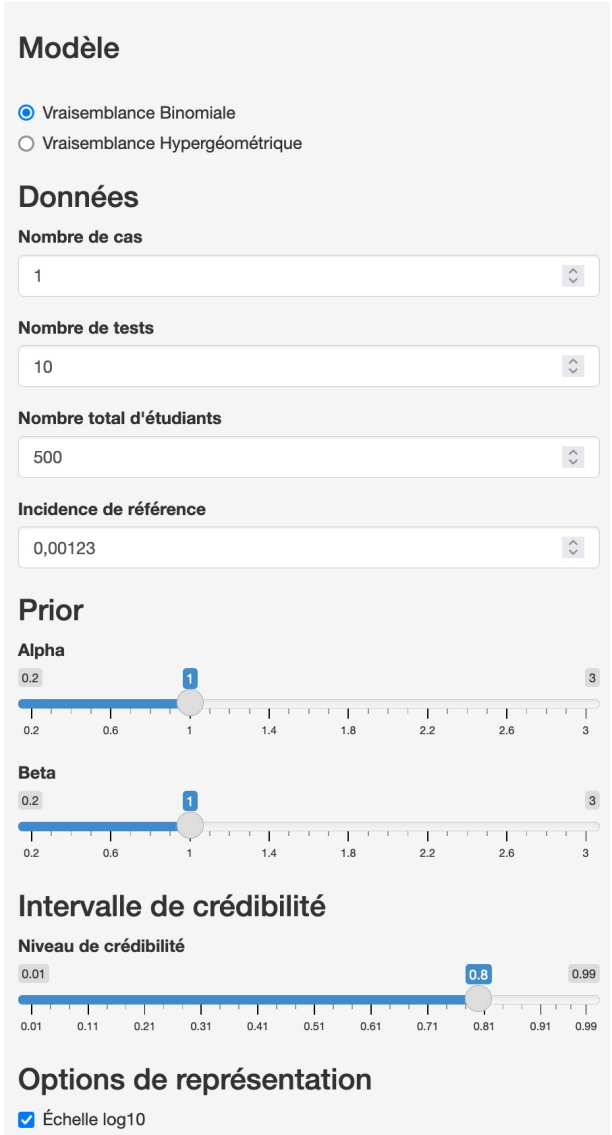
Methods: An international, open-label, adaptive randomized controlled trial. Using a Bayesian framework, the trial will declare results as soon as pre-specified posterior probabilities for superiority, futility, or harm are reached. The trial uses response-adaptive randomization to maximize the probability that patients will receive the more beneficial treatment approach, as treatment effect information accumulates within the trial. By leveraging a common data safety monitoring

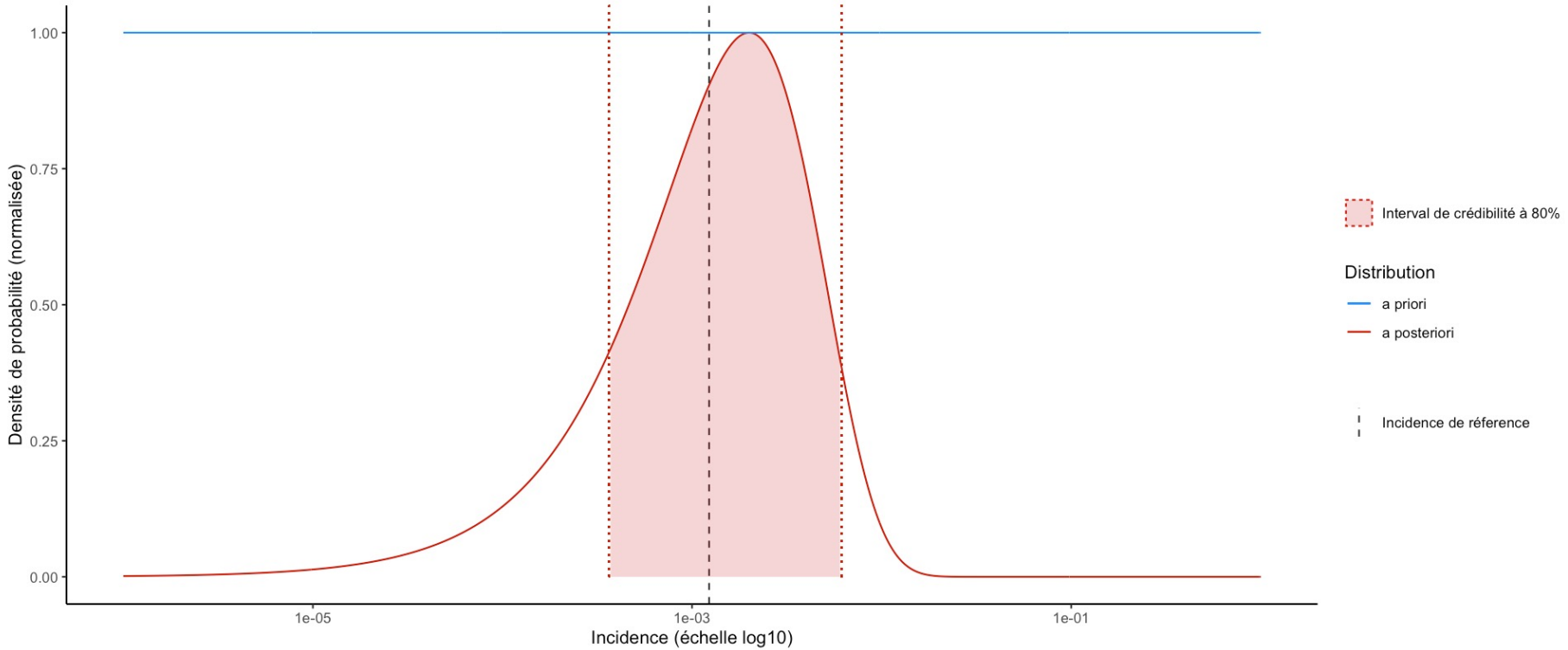
Projets 2020

1. Ré-analyse bayésienne de la méta-analyse sur le traitement de la COVID-19 par hydroxychloroquine présentée dans l'article de Fiolet *et al.*
2. Ré-analyse bayésienne de la méta-analyse sur les performances tests antigéniques pour détecter le SARS à partir de la Synthèse de la Haute Autorité de Santé du 8 octobre 2020
3. Estimation bayésienne de la prévalence de la COVID-19 en Islande et aux États-Unis à partir de l'article de Gao & Dong
4. Ré-analyse bayésienne de l'étude de Bendavid *et al.* sur la séroprévalence d'anticorps au SARS-CoV-2 en Californie à partir de l'article de Gelman & Carpenter

- Thibault Fiolet et al., "Effect of Hydroxychloroquine with or Without Azithromycin on the Mortality of Coronavirus Disease 2019 (Covid-19) Patients: A Systematic Review and Meta-Analysis," *Clinical Microbiology and Infection*, 2020, in press, doi:10.1016/j.cmi.2020.08.022.
- Haute Autorité de Santé, "Revue Rapide Sur Les Tests de Détection Antigénique Du Virus Sars-Cov-2," 2020, https://www.has-sante.fr/jcms/p_3213483/fr/revue-rapide-sur-les-tests-de-detection-antigenique-du-virus-sars-cov-2.
- Xiang Gao and Qunfeng Dong, "A Primer on Bayesian Estimation of Prevalence of Covid-19 Patient Outcomes," *JAMIA Open*, November 2020, 2574–31, doi:10.1093/jamiaopen/ooaa062.
- Eran Bendavid et al., "COVID-19 Antibody Seroprevalence in Santa Clara County, California," *medRxiv*, 2020, 2020.04.14.20062463, doi:10.1101/2020.04.14.20062463.
- Andrew Gelman and Bob Carpenter, "Bayesian Analysis of Tests with Unknown Specificity and Sensitivity," *Journal of the Royal Statistical Society: Series C (Applied Statistics)* 69, no. 5 (2020): 1269–83, doi:10.1111/rssc.12435.

Monitoring du taux de positivité au test PCR du SARS-Cov-2 à l'Université de Bordeaux





Indicateur	Valeur pour 100 000	Facteur de Bayes
Intervalle de crédibilité à 80%	[32.21 ; 613.18]	
Maximum a posteriori	200	1.11 (différence anecdotique)
Médiane a posteriori	335.5	0.94 (inférieur à la référence)
Moyenne a posteriori	398.41	0.82 (inférieur à la référence)

https://shiny-u-bordeaux-covidsurv.apps.math.cnrs.fr/

Réflexions

Pandémie : fatigue ?

Un regain de motivation ?

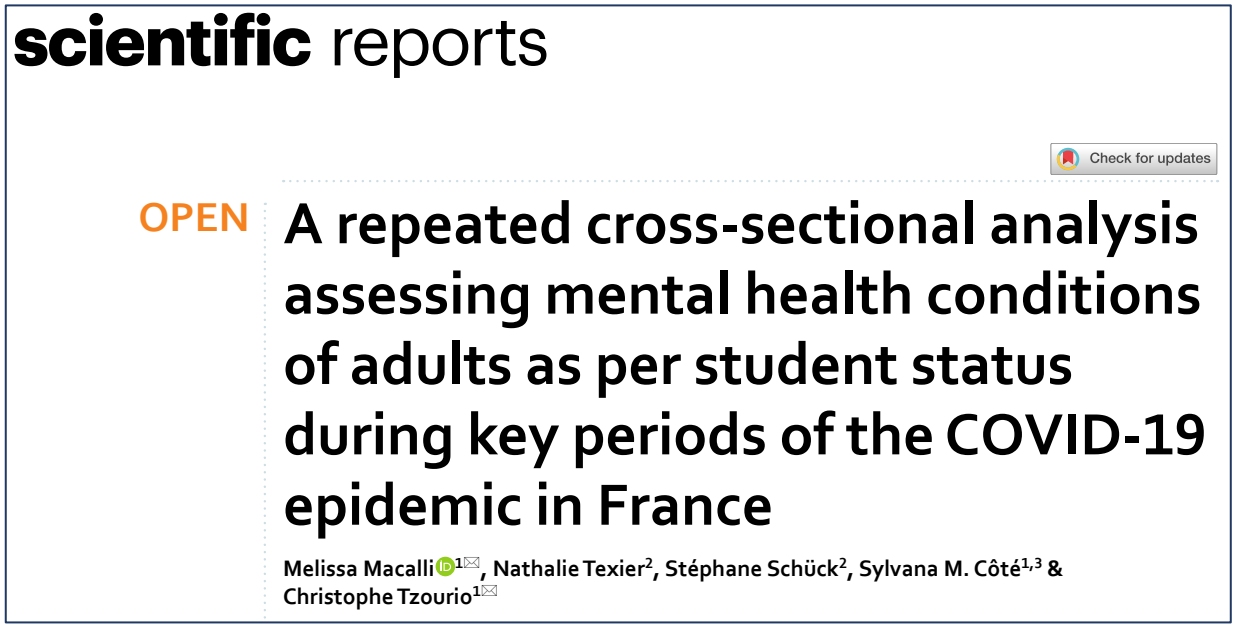
- **Enseignant :** (très) enthousiaste à l'idée de montrer l'utilité de ces méthodes sur un sujet actuel, connu de tous, au cœur des préoccupations de chacun

- **Les étudiants :** aucun enthousiasme particulier, pas de motivation ou d'implication particulière détectée en classe, ou dans les questionnaires de retour

Impact psychologique de la pandémie sur les étudiants

e-cohorte CONFINS :

- symptomes depressifs ↗
- anxiété ↗



Sujet d'actualité : 😊 & 😟

- Intérêt accru des étudiants, plus concernés. Vraiment ??
- ⇒ Lassitude/saturation, mélange des genres (Amphi VS BFM)

Merci

SISTM team

🚨🚨 ***We have postdoc, PhD student, engineer & intern openings !!***

boris.hejblum@u-bordeaux.fr
rodolphe.thiebaut@u-bordeaux.fr
https://www.inria.fr/sistm
http://borishejblum.science