

# Theoretical statistics in practice

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Nancy Reid  
University of Toronto

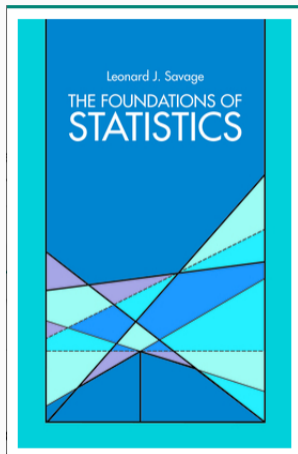
October 13 2023



1. Theory and Foundations
2. Applications
3. Back to Theory

# **Theory and Foundations**

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*It is unanimously agreed that statistics depends somehow on probability. But, as to what probability is and how it is connected with statistics, there has seldom been such complete disagreement and breakdown of communication since the Tower of Babel. Doubtless, much of the disagreement is merely terminological and would disappear under sufficiently sharp analysis.*

- Statistics needs a healthy interplay between theory and applications
- theory meaning **foundations**, rather than theoretical analysis of specific techniques
- must be continually tested against new applications
- “the practical application of general theorems is a different art from their establishment by mathematical proof”

Fisher 1958 SMRW



International Statistical Review

*International Statistical Review* (2015), 83, 2, 293–308 doi:10.1111/insr.12067

### **On Some Principles of Statistical Inference**

**Nancy Reid<sup>1</sup> and David R. Cox<sup>2</sup>**

## ... theory and foundations of statistics

- probability, analysis, applied mathematics modelling
- Bayes, Neyman, Fisher approaches to inference
- nature of uncertainty epistemic, empirical
- nature of induction belief functions, inferential models
- interpretation of  $p$ -values, confidence regions, credibility intervals, likelihood ratios
- role of sufficiency, ancillarity, conditioning, asymptotic theory
- sparsity, causality, assumption-free/lean inference, stability, prediction, decisions

## What use are foundations?

- provide a rigorous basis for the development of techniques
- provide a common language for particular classes of problems
- help to clarify the nature of uncertainty in scientific conclusions
- highlight aspects of data analysis which are likely to raise difficult issues
- suggest strategies for tackling highly complex problems
- avoid 're-inventing the wheel' for each new application

# Applications

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## Climate Change Made East Africa's Drought 100 Times as Likely, Study Says

The findings starkly show the misery that the burning of fossil fuels, mostly by rich countries, inflicts on societies that emit almost nothing by comparison.



NY Times, April 27



A water well near the town of Kelafo in Ethiopia, one of the nations hit hardest by the

## Human-induced climate change increased drought severity in Horn of Africa

World Weather Attribution, April 27

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10. Wenchang Yang, *Department of Geosciences, Princeton University, Princeton, NJ 08544, USA*
11. Sihan Li, *Department of Geography, University of Sheffield*
12. Maja Vahlberg, *Red Cross Red Crescent Climate Centre, The Hague, the Netherlands*
13. Roop Singh, *Red Cross Red Crescent Climate Centre, The Hague, the Netherlands*
14. Dorothy Heinrich, *Red Cross Red Crescent Climate Centre, The Hague, the Netherlands*
15. Carolina Marghidian Pereira, *Faculty of Geo-Information Science and Earth Observation (ITC), University of Twente, Enschede, the Netherlands; Red Cross Red Crescent Climate Centre, The Hague, the Netherlands*
16. Julie Arrighi, *Red Cross Red Crescent Climate Centre, The Hague, the Netherlands; Global Disaster Preparedness Center, Washington DC, USA; University of Twente, The Netherlands*
17. Lisa Thalheimer, *United Nations University, Institute for Environment and Human Security, Bonn, Germany*
18. Cheikh Kane, *Red Cross Red Crescent Climate Centre, The Hague, the Netherlands; Institut de Recherche pour le Développement, U01000/99AA01, Marseille, France*
19. Friederike E. L. Otto, *Grantham Institute, Imperial College London, UK*

### Main findings



HEALTH AND SCIENCE

### Ivermectin — a drug once touted as a Covid treatment by conservatives — doesn't improve recovery much, clinical trial finds

PUBLISHED MON, OCT 24 2022-3:27 PM EDT | UPDATED TUE, OCT 25 2022-3:49 PM EDT





MARKETS BUSINESS INVESTING TECH POLITICS CNBC TV

HEALTH AND SCIENCE

## Ivermectin — a drug once touted as a Covid treatment by conservatives — doesn't improve recovery much, clinical trial finds

PUBLISHED MON, OCT 24 2022 3:27 PM EDT | UPDATED TUE, OCT 25 2022 3:49 PM EDT



Research

JAMA | [Original Investigation](#)

## Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19 A Randomized Clinical Trial

Susanna Naggie, MD, MHS; David R. Boulware, MD, MPH; Christopher J. Lindsell, PhD; Thomas G. Stewart, PhD; Nina Gentile, MD; Sean Collins, MD, MSc; Matthew William McCarthy, MD; Dushyantha Jayaweera, MD; Mario Castro, MD, MPH; Mark Sulkowski, MD; Kathleen McTigue, MD, MPH, MS; Florence Thacklin; G. Michael Felker, MD, MHS; Adit A. Ginde, MD, MPH; Carolyn T. Bramante, MD, MPH; Alex J. Slandzicki, MD; Ahab Gabriel, MD; Nirav S. Shah, MD, MPH; Leslie A. Lenert, MD, MS; Sarah E. Dunsmore, PhD; Stacey J. Adam, PhD; Allison DeLong, BS; George Hanna, MD; April Remaly, BA; Rhonda Wilder, MS; Sybil Wilson, RN; Elizabeth Shenkman, PhD; Adrian F. Hernandez, MD, MHS; for the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-6) Study Group and Investigators

The screenshot shows the user interface for the 'Uncharted with Hannah Fry' podcast on the BBC Radio 4 app. The top navigation bar includes 'Home', 'Episodes', and 'Podcast'. The main content area features a large orange-themed image of Hannah Fry pointing upwards, with the text 'UNCHARTED with Hannah Fry' and a '4' in a circle. A 'Listen now' button is visible. Below the image, the episode title '9. Access Denied' is displayed, followed by a short description: 'A young researcher gains access to a secretive data set and discovers something shocking. What happens when a system designed to help people harms them instead?'. The episode is marked as 'Available now' and has a duration of '14 minutes'. A 'Download' button is located at the bottom left. On the right side, the 'Last on' section shows the broadcast time 'Last Thursday 13:45' on 'BBC RADIO 4'. The 'More episodes' section lists '8. In the Habit' as the previous episode and '10. Devil in the Detail' as the next episode, each with a speaker icon. A link to 'See all episodes from Uncharted with Hannah Fry' is also present.

**BBC RADIO 4** Uncharted with Hannah Fry

Home Episodes Podcast

**UNCHARTED** with Hannah Fry **4**

Listen now

**9. Access Denied**

A young researcher gains access to a secretive data set and discovers something shocking. What happens when a system designed to help people harms them instead?

Available now 14 minutes

Show more

Download

**Last on**

**BBC RADIO 4** Last Thursday 13:45 BBC RADIO 4

**More episodes**

**PREVIOUS**  
8. In the Habit

**NEXT**  
10. Devil in the Detail

See all episodes from Uncharted with Hannah Fry

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The article header features the 'Science' logo with the AAAS emblem. Below the logo is a photograph of two women, one Black and one white, both wearing glasses and white lab coats, looking at a tablet together. To the right of the photo is a text box that reads: 'Racial bias in cost data leads an algorithm to underestimate health care needs of Black patients.'

### SOCIAL SCIENCE

## Assessing risk, automating racism

A health care algorithm reflects underlying racial bias in society

By **Ruha Benjamin**

**A**s more organizations and industries adopt digital tools to identify

era, the intention to deepen racial inequities was more explicit, today coded inequity is perpetuated precisely because those who design and adopt such tools are not

beyond the algorithm developers by constructing a more fine-grained measure of health outcomes, by extracting and cleaning data from electronic health records to

## RESEARCH

## RESEARCH ARTICLE

## ECONOMICS

## Dissecting racial bias in an algorithm used to manage the health of populations

Ziad Obermeyer<sup>1,2</sup>, Brian Powers<sup>3</sup>, Christine Vogeli<sup>4</sup>, Senthil Mullainathan<sup>2†</sup>

Health systems rely on commercial prediction algorithms to identify and help patients with complex health needs. We show that a widely used algorithm, typical of this industry-wide approach and affecting millions of patients, exhibits significant racial bias: At a given risk score, Black patients are considerably sicker than White patients, as evidenced by signs of uncontrolled illnesses. Remedying this disparity would increase the percentage of Black patients receiving additional help from 17.7 to 46.5%. The bias arises because the algorithm predicts health care costs rather than illness, but unequal access to care means that we spend less money caring for Black patients than for White patients. Thus, despite health care cost appearing to be an effective proxy for health by some measures of predictive accuracy, large racial biases arise. We suggest that the choice of convenient, seemingly effective proxies for ground truth can be an important source of algorithmic bias in many contexts.

There is growing concern that algorithms may reproduce racial and gender disparities via the people building them or through the data used to train them (1-3). Empirical work is increasingly lending support to these concerns. For example, job search ads for highly paid positions are less likely to be presented to women (4), searches

researcher-created algorithms (10-13). Without an algorithm's training data, objective function, and prediction methodology, we can only guess as to the actual mechanisms for the important algorithmic disparities that arise. In this study, we exploit a rich dataset that provides insight into a live, scaled algorithm deployed nationwide today. It is one of the largest and most trusted examples of a class

that rely on past data to build a predictor of future health care needs.

Our dataset describes one such typical algorithm. It contains both the algorithm's predictions as well as the data needed to understand its inner workings: that is, the underlying ingredients used to form the algorithm (data, objective function, etc.) and links to a rich set of outcome data. Because we have the inputs, outputs, and eventual outcomes, our data allow us a rare opportunity to quantify racial disparities in algorithms and isolate the mechanisms by which they arise. It should be emphasized that this algorithm is not unique.

Rather, it is emblematic of a generalized approach to risk prediction in the health sector, widely adopted by a range of for- and non-profit medical centers and governmental agencies (2).

Our analysis has implications beyond what we learn about this particular algorithm. First, the specific problem solved by this algorithm has analogies in many other sectors: The predicted risk of some future outcome (in our case, health care needs) is widely used to target policy interventions under the assumption that the treatment effect is monotonic in that risk, and the methods used to build the algorithm are standard. Mechanisms of bias uncovered in this study likely operate elsewhere. Second, even beyond our particular finding, we hope that this exercise illustrates the importance, and the large opportunity, of studies

Science  
AAAS

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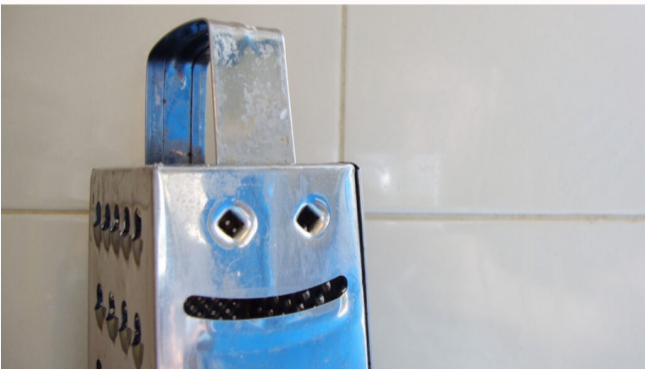
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NEWS

NEUROSCIENCE

## Americans tend to assume imaginary faces are male

Why people perceive faces in inanimate objects as male by default is still unclear



<sup>2</sup>People often see imaginary faces in everyday objects, such as this smiling face in a cheese grater. These faces were more often seen as male than female by U.S. adults in a new survey.

<sup>3</sup>AUL DAVID GALVIN/MOMENT/GETTY IMAGES PLUS



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PNAS

Proceedings of the  
National Academy of Sciences  
of the United States of America

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TORONTO

Keyword, A

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### RESEARCH ARTICLE

## Illusory faces are more likely to be perceived as male than female

 Susan G. Wardle,  Sanika Paranjape,  Jessica Taubert, and  Chris I. Baker

[+ See all authors and affiliations](#)

# Linking theory with practice

1. **Drought** Climate change attribution  
climate models, subgroup analyses, predictions
2. **Covid** Treatment with Ivermectin  
randomized trial, proportional hazards regression, Bayes/frequentist
3. **Health Care** Predicting high-needs patients  
algorithmic bias, variable selection
4. **Faces** Human perception  
sign test, regression, computational modelling

# Applications

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**Drought**



NEWS

Science

## Deadly African drought not possible without climate change, study finds



Warming climate made long rains twice as likely to underdeliver, World Weather Attribution calculates

Thomson Reuters · Posted: Apr 27, 2023 8:43 AM EDT | Last Updated: April 27



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## Global warming made Horn of Africa drought possible: WWA study

*World Weather Attribution scientists say rising greenhouse gas emissions made the nearly 3-year drought at least 100 times more likely.*

Dwivedi Memorial Lecture October 2023

## Climate Change Made East Africa's Drought 100 Times as Likely, Study Says

The findings starkly show the misery that the burning of fossil fuels, mostly by rich countries, inflicts on societies that emit almost nothing by comparison.

Give this article



A water well near the town of Kelafo in Ethiopia, one of the nations hit hardest by the drought. Eduardo Soteras/Agence France-Presse — Getty Images

## Human-induced climate change increased drought severity in Horn of Africa

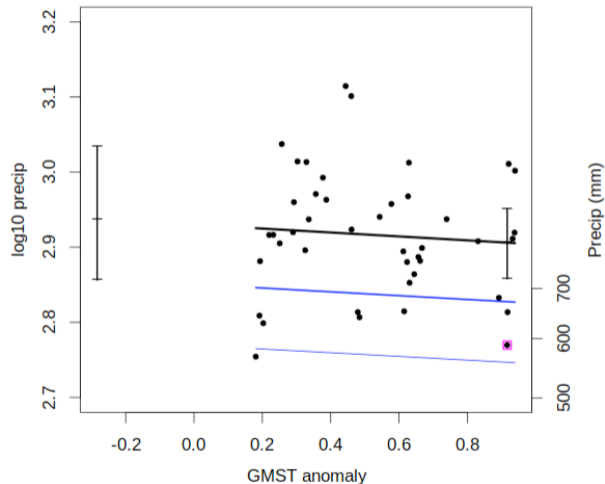
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- **observational** data, 3 sources
  1. global daily rainfall & temperature 0.5° × 0.5°, 1979 –
  2. daily rainfall infra-red, “SoA”, 1981 –
  3. monthly rainfall 1981–2014
- 4-year smoothed mean surface temperature proxy for anthropogenic climate change
- climate modelling data, 4 sources
  1. combine 12 global and 8 climate models: resolution 0.44° 29 sims
  2. combine 5 global and 4 climate models: resolution 0.22° 10 sims
  3. atmosphere-ocean coupled GCMs (two) 10/3 simulations
  4. sea-surface temperature forced ensemble, high resolution 11 simulations
- thanks to Whitney Huang for many clarifications

- response is  $\log_{10}$ (monthly rainfall) in 2021 and 2022  
and  $\log_{10}$ (PET) – potential evapotranspiration
  - covariates are global temperature anomaly, and ENSO index  
El Nino-Southern Oscillation
  - “As a measure of anthropogenic climate change we use smoothed GMST”  
Global Mean Surface Temperature
  - “Methods for observational and model analysis ... and synthesis are used according to the World Weather Attribution Protocol”  
Philip et al. 2020
1. trend using observational data
  2. find climate models consistent with 1.
  3. compare predictions from 1. and 2.
  4. synthesize results in 3. to provide conclusions

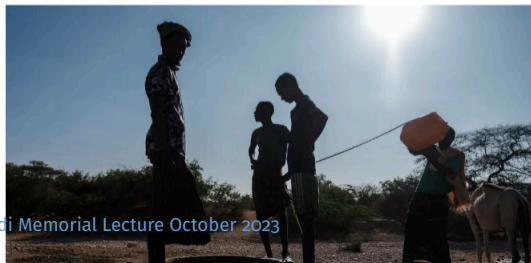


- rainfall decreasing with increasing temperature  
but not much
- 2022 rainfall is about a 1 in 20 year event
- 2022 drought about **2 times** more likely under climate change
- uncertainty 0.1 — 360



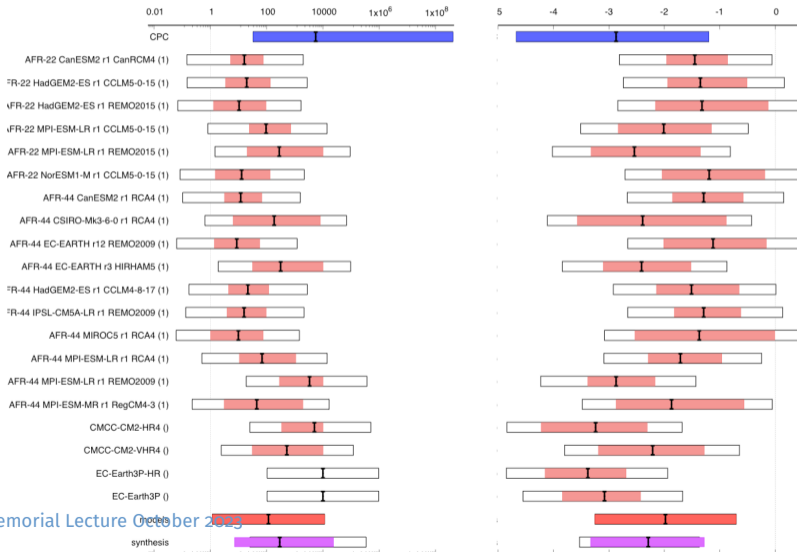
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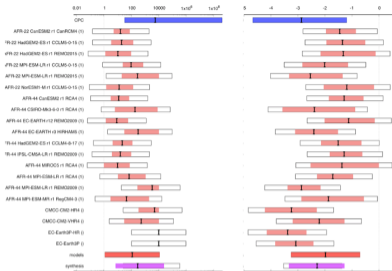
- change the response to SPEI rainfall adjusted for evaporation
- 2022 drought now **5500** times more likely  
uncertainty  $32 \text{ to } 4 \times 10^8$
- consider 'long rains' and 'short rains' separately MAM, OND
- combine model simulation results with observational data

**(a) Probability Ratio (left) and Intensity change (right) for current vs. 1.2degC cooler climates**

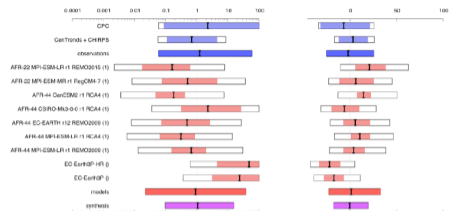


precipitation  
adjusted  
for evaporation

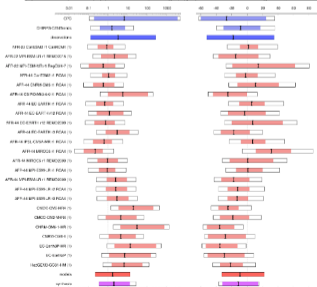
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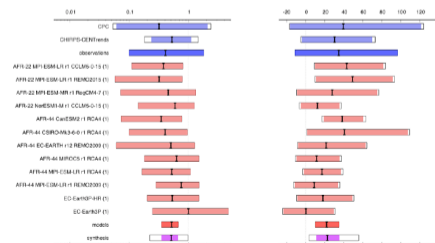
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forest plots

- extrapolation beyond observations  
extreme value modelling
- assigning uncertainty to combined results  
sources of uncertainty
- ratios of **estimated** probabilities  
nearly unbounded confidence intervals
- **selection of events** for analysis
- joint modelling of precipitation and evapotranspiration  
tail copula modelling

Stein *Statist. Sci.* 2019

Senn 2020

Cox & Hinkley 1974

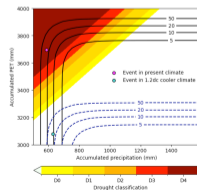
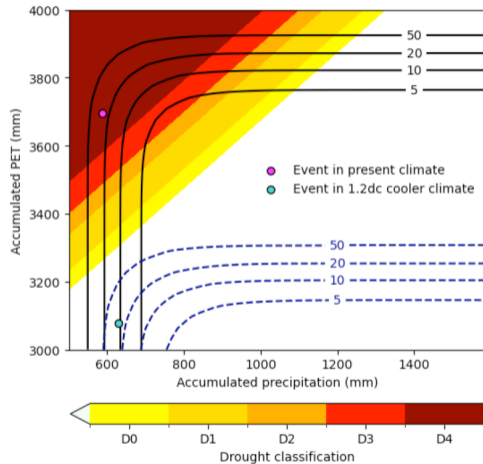


Figure 3: Joint distribution of 2-month precip and PET with corresponding SPEI drought classification (CPC dataset). The solid contours indicate return periods under the joint distribution in the current climate, while the dashed contours indicate the same return periods in a 1.2°C cooler climate. The shaded contours represent different levels of drought severity. The magenta point indicates the 2022 drought event in the current climate, with a 100-year return period of 26 years (uncertainty, 22–37 years), while the cyan point shows an event of the

## Aside: joint modelling



**Figure 3:** Joint distribution of 24-month precip and PET with corresponding SPEI drought classification (CPC Dataset). The solid contours indicate return periods under the joint distribution in the current climate, while the dashed contours indicate the same return periods in a 1.2°C cooler climate. The shaded contours represent different levels of drought severity. The magenta point indicates the 2022 drought event in the current climate



On average, wildfires burn about 2.5 million hectares in Canada each year. In 2023, wildfires have already burned nearly 14 million hectares. Photo by Audrey Marcoux, SOPFEU.

Home > Wildfire > Climate change more than doubled the likelihood of extreme fire weather conditions in Eastern Canada

## Climate change more than doubled the likelihood of extreme fire weather conditions in Eastern Canada

22 August, 2023

During May and June 2023 Canada witnessed exceptionally extreme fire-weather conditions, leading to extensive wildfires that burned over 13 million

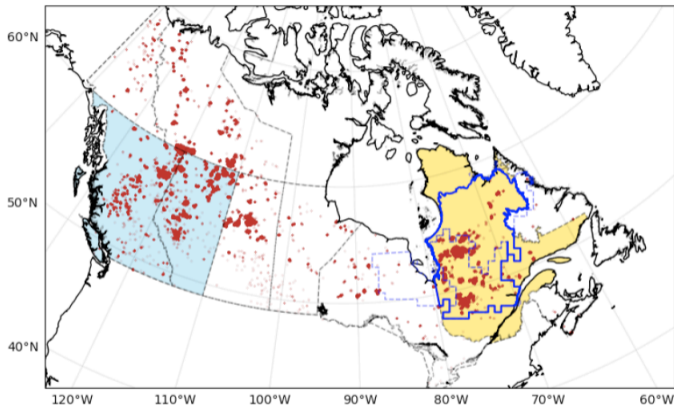
### Full study

- Download the full study: Climate change more than doubled the likelihood of extreme fire weather conditions in Eastern Canada (26 pages, 1.8MB)

### Main findings

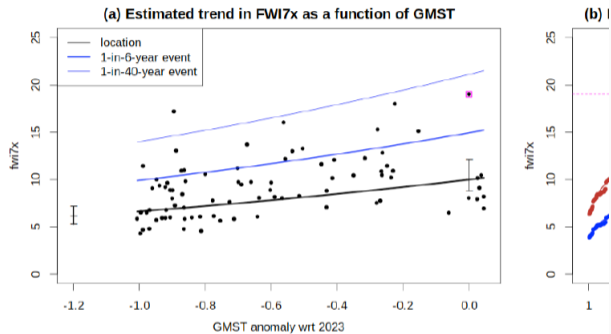
- Fire weather is one important condition driving wildfires, although changes in vegetation (wildfire fuel), ignition factors, and fire management strategies also contribute to future wildfire risk.
- In today's climate, intense fire weather like that observed in May-July 2023 is a moderately extreme event, expected to occur once every 20-25 years. This means in any given year such an event is expected with 4-5% probability.
- Climate change made the cumulative severity of Québec's 2023 fire season to the end of July around 50% more intense, and seasons of this severity at least seven times more likely to occur. Peak fire weather (FWI7x) like that experienced this year is at least twice as likely, and the intensity has increased by about 20% due to human-induced climate change.
- Observed changes are typically larger than in the models.
- As expected, likelihood and intensity are projected to increase further in a 2°C warmer world.
- Changes in fire weather are associated with an increase in temperature and decrease in humidity, both of which are driven by human-induced warming; the effect was compounded in 2023 by unusually low precipitation
- The extent, magnitude, and location of concomitant wildfires posed significant challenges for wildfire management which largely focused on disaster response and wildfire containment to limit the impact on lives and infrastructure.
- The wildfires had disproportionate impacts on indigenous, fly-in, and other remote communities who were particularly vulnerable due to lack of services and barriers to response interventions.
- The consequences from the wildfires reached far beyond the burned areas with displaced impacts due to air pollution threatening health, mobility, and economic activities of people across North America.
- As fire weather risks increase, changes in fire management strategies and increased resources will be required to meet the increased challenges.

“peak fire weather ...  
at least twice as likely”

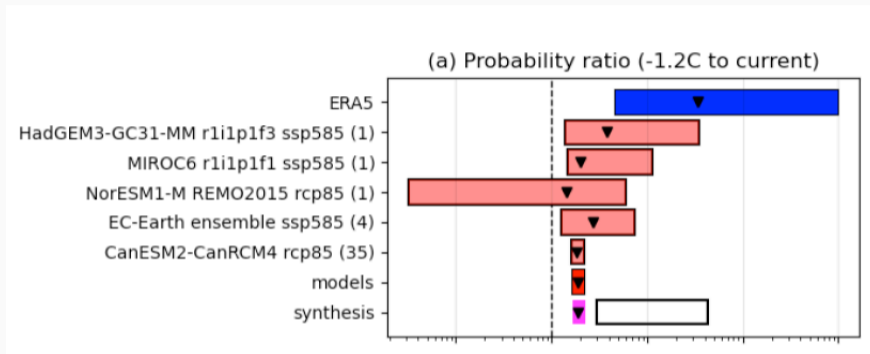


**Figure 1:** Red dots mark active fires from January-July 2023 identified with high confidence (>80%) in the MCD14DL MODIS Active Fire and Thermal Anomalies product. The heavily impacted provinces of Alberta and Saskatchewan are highlighted with a blue outline.





**Figure 7:** (a) Linear trend in ERA5 FWI7x as a function of GMST. parameter of the fitted distribution, and the blue lines show estimation lines show the 95% confidence interval for the location parameter



“data”: 34 times as likely (4.7,  $\infty$ )

models: 1.9 times as likely (1.66, 2.24)

# Applications

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**Medicine**

## Ivermectin — a drug once touted as a Covid treatment by conservatives — doesn't improve recovery much, clinical trial finds

PUBLISHED MON, OCT 24 2022 3:27 PM EDT | UPDATED TUE, OCT 25 2022 3:49 PM EDT



### Research

JAMA | [Original Investigation](#)

## Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19 A Randomized Clinical Trial

Susanna Naggie, MD, MHS; David R. Boulware, MD, MPH; Christopher J. Lindsell, PhD; Thomas G. Stewart, PhD; Nina Gentile, MD; Sean Collins, MD, MSc; Matthew William McCarthy, MD; Dushyantha Jayaweera, MD; Mario Castro, MD, MPH; Mark Sulkowski, MD; Kathleen McTigue, MD, MPH, MS; Florence Thickett; G. Michael Felker, MD, MHS; Adit A. Ginde, MD, MPH; Carolyn T. Bramante, MD, MPH; Alex J. Slandzicki, MD; Ahab Gabriel, MD; Nirav S. Shah, MD, MPH; Leslie A. Lenert, MD, MS; Sarah E. Dunsmore, PhD; Stacey J. Adam, PhD; Allison DeLong, BS; George Hanna, MD; April Remaly, BA; Rhonda Wilder, MS; Sybil Wilson, RN; Elizabeth Shenkman, PhD; Adrian F. Hernandez, MD, MHS; for the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-6) Study Group and Investigators

## Research

JAMA | **Original Investigation**

# Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19

## A Randomized Clinical Trial

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- randomized controlled trial
- **platform trial** of 6 potential treatments multicenter
- analysis of each treatment uses the same placebo group
  
- 817 patients in treatment arm; 774 in control arm
- primary outcome: time to recovery
- explanatory variables: **treatment**, age, sex, prior symptoms, calendar time, vaccination status, geographic region, center, baseline severity and others

- Bayesian proportional hazards model

$$\lambda(t; \mathbf{x}) = \lambda_0(t) \exp(\beta_0 + \beta_1 \mathbf{x}_1 + \beta_2 \mathbf{x}_2 + \dots + \beta_p \mathbf{x}_p)$$

- some covariates fit with splines e.g. age
- underlying hazard modelled parametrically e.g. Weibull, or splines
- prior distributions:
  - for parameters of hazard function
  - for coefficients for explanatory variables  $\beta_0, \beta_2, \dots, \beta_p$
  - **for  $\beta_1$  – treatment** skeptical, noninformative, none
- likelihood  $\times$  prior  $\longrightarrow$  posterior  $\longrightarrow$  marginal posterior for  $\beta_1$  or  $\exp(\beta_1)$

## Aside: the analysis

- model for data represented by density function

$$f(\mathbf{y} \mid \theta; \mathbf{x})$$

also called the likelihood function for  $\theta$

- Bayesian analysis defines a prior density for  $\theta$

$$\pi(\theta)$$

- rules of conditional probability applied to give posterior density for  $\theta$ :

$$\pi(\theta \mid \mathbf{y}; \mathbf{x}) = \frac{f(\mathbf{y} \mid \theta; \mathbf{x})\pi(\theta)}{\int f(\mathbf{y} \mid \theta; \mathbf{x})\pi(\theta)d\theta} \propto f(\mathbf{y} \mid \theta; \mathbf{x})\pi(\theta)$$

- posterior marginal density for parameter of interest  $\psi(\theta)$ :

$$\pi_{\text{marg}}(\psi \mid \mathbf{y}; \mathbf{x}) = \int_{\{\psi(\theta)=\psi\}} \pi(\theta \mid \mathbf{y}; \mathbf{x})d\theta$$



## Key Points

**Question** Does ivermectin, 400 µg/kg, daily for 3 days, compared with placebo, shorten symptom duration among adult ( $\geq 30$  years) outpatients in the US with symptomatic mild to moderate COVID-19?

**Findings** In this double-blinded, randomized, placebo-controlled platform trial conducted in the US during a period of Delta and Omicron variant predominance, and that included 1591 adult outpatients with COVID-19, the posterior probability of improvement in time to recovery in those treated with ivermectin vs placebo had a hazard ratio of 1.07, with a posterior probability of benefit of .91. This did not meet the prespecified threshold of posterior probability greater than .95.

**Meaning** These findings do not support the use of ivermectin in outpatients with mild to moderate COVID-19.

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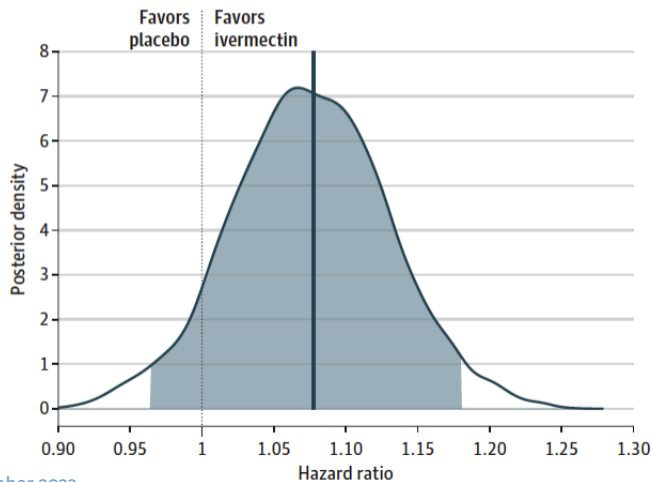
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**Meaning** These findings do not support the use of ivermectin in outpatients with mild to moderate COVID-19.

“Among outpatients with mild to moderate COVID-19, treatment with ivermectin, compared with placebo, did not **significantly** improve time to recovery.”

Hazard ratio estimated at 1.07, with posterior probability that  $HR > 1 = 0.91$

“This did not meet the prespecified threshold of posterior probability greater than 0.95”

**A** Days to sustained recovery

# The theory: modelling and conditional inference

- Cox 1972: On regression models and life tables
- sets out proportional hazards regression and non-proportional

$$\lambda(t; \mathbf{x}) = \lambda_0(t) \exp(\mathbf{x}^T \beta)$$

hazard function = density function / (1 - distribution function)

- proposes analysis via **partial likelihood** eliminates hazard function
- uses point process modelling + conditional inference

- full likelihood function  $L(\beta, \lambda) \propto \prod_{j=1}^n \{ \lambda_0(t_j) \exp(\mathbf{x}_j^T \beta) \}^{\delta_j} \exp\{ - \exp(\mathbf{x}_j^T \beta) \Lambda_0(t_j) \}$

- partial likelihood function  $L_{part}(\beta) \propto \prod_{failures} \frac{\exp(\mathbf{x}_j^T \beta)}{\sum_{k \in \mathcal{R}_j} \exp(\mathbf{x}_k^T \beta)}$

# The theory: Bayes and frequentist

Research Original Investigation

Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19

Table 2. Primary and Secondary Outcomes

	Group, No. (%)		Adjusted estimate (95% CrI) <sup>a</sup>	Posterior P value (efficacy)
	Ivermectin	Placebo		
No.	817	774		
Primary end point, time to recovery <sup>b</sup>				
Skeptical prior (primary analysis)			HR, 1.07 (0.96 to 1.17)	.91
Noninformative prior (sensitivity analysis)			HR, 1.09 (0.97 to 1.22)	.93
No prior (sensitivity analysis)			HR, 1.09 (0.98 to 1.22) <sup>c</sup>	

Skeptical prior	1.07	(0.96 – 1.17)	0.91
Noninformative prior	1.09	(0.97 – 1.22)	0.93
No prior	1.09	(0.98 – 1.22)	

# The theory: Bayes and frequentist

- both methods **often** lead to the same conclusions **but not always**
- [Wasserman 2015; 2022](#) very helpful overviews
  - Stein 1959
  - Stone 1970
  - Robins and Ritov 1997
  - ...
- the nature of the conclusions is **different**
  - probability representing **degree of uncertainty** epistemic
  - probability representing **long-run frequency** aleatory
- calibration of Bayesian inference assesses the first on the basis of the second Cox 1958, BFF

## Wedding Bayesian and Frequentist Designs Created a Mess

[Code](#)

2023

INFERENCE

RCT

BAYES

DESIGN

EVIDENCE

MULTIPLICITY

POSTERIOR

PRIOR

SEQUENTIAL

This article describes a real example in which use of a hybrid Bayesian-frequentist RCT design resulted in an analytical mess after overly successful participant recruitment.

AUTHOR

**Frank Harrell**

AFFILIATION

Department of Biostatistics  
Vanderbilt University School of Medicine

PUBLISHED

August 22, 2023

<https://www.fharrell.com/post/hybrid/>

# Applications

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**Health Care**



The screenshot shows the BBC Radio 4 podcast player interface. At the top, it says 'ADIO 4 Uncharted with Hannah Fry'. Below this are navigation tabs for 'Home', 'Episodes', and 'Podcast'. The main content area features a large orange and black image of Hannah Fry pointing at a screen with the text 'UNCHARTED with Hannah Fry' and a '4' in a circle. A 'Listen now' button is visible. Below the image, the episode title '9. Access Denied' is displayed, followed by a short description: 'A young researcher gains access to a secretive data set and discovers something shocking. What happens when a system designed to help people harms them instead?'. It also indicates 'Available now' and '14 minutes'. A 'Download' button is at the bottom left. On the right side, there is a 'Last on' section showing 'Last Thursday 13:45 BBC RADIO 4' and a 'More episodes' section with 'PREVIOUS 8. In the Habit' and 'NEXT 10. Devil in the Detail'.

The article header features the 'Science' logo with the AAAS symbol below it. Below the logo is a photograph of two women in a clinical setting; one is a Black woman with glasses and the other is a white woman with glasses and a stethoscope. To the right of the photo, a text box reads: 'Racial bias in cost data leads an algorithm to underestimate health care needs of Black patients.'

### SOCIAL SCIENCE

## Assessing risk, automating racism

A health care algorithm reflects underlying racial bias in society

By **Ruha Benjamin**

**A**s more organizations and industries adopt digital tools to identify

era, the intention to deepen racial inequities was more explicit, today coded inequity is perpetuated precisely because those who design and adopt such tools are not

beyond the algorithm developers by constructing a more fine-grained measure of health outcomes, by extracting and cleaning data from electronic health records to

## RESEARCH

## RESEARCH ARTICLE

## ECONOMICS

## Dissecting racial bias in an algorithm used to manage the health of populations

Ziad Obermeyer<sup>1,2\*</sup>, Brian Powers<sup>3</sup>, Christine Vogeli<sup>4</sup>, Sendhil Mullainathan<sup>5\*\*†</sup>

Health systems rely on commercial prediction algorithms to identify and help patients with complex health needs. We show that a widely used algorithm, typical of this industry-wide approach and affecting millions of patients, exhibits significant racial bias: At a given risk score, Black patients are considerably sicker than White patients, as evidenced by signs of uncontrolled illnesses. Remedying this disparity would increase the percentage of Black patients receiving additional help from 17.7 to 46.5%. The bias arises because the algorithm predicts health care costs rather than illness, but unequal access to care means that we spend less money caring for Black patients than for White patients. Thus, despite health care cost appearing to be an effective proxy for health by some measures of predictive accuracy, large racial biases arise. We suggest that the choice of convenient, seemingly effective proxies for ground truth can be an important source of algorithmic bias in many contexts.

There is growing concern that algorithms may reproduce racial and gender disparities via the people building them or through the data used to train them (1–3). Empirical work is increasingly lending support to these concerns. For example, job search ads for highly paid positions are less

researcher-created algorithms (10–13). Without an algorithm's training data, objective function, and prediction methodology, we can only guess as to the actual mechanisms for the important algorithmic disparities that arise.

In this study, we exploit a rich dataset that provides insight into a live, scaled algorithm

that rely on past data to build a predictor of future health care needs.

Our dataset describes one such typical algorithm. It contains both the algorithm's predictions as well as the data needed to understand its inner workings: that is, the underlying ingredients used to form the algorithm (data, objective function, etc.) and links to a rich set of outcome data. Because we have the inputs, outputs, and eventual outcomes, our data allow us a rare opportunity to quantify racial disparities in algorithms and isolate the mechanisms by which they arise. It should be emphasized that this algorithm is not unique. Rather, it is emblematic of a generalized approach to risk prediction in the health sector, widely adopted by a range of for- and non-profit medical centers and governmental agencies (21).

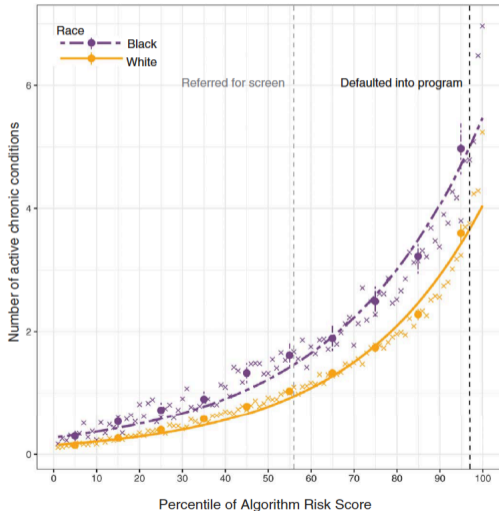
Our analysis has implications beyond what we learn about this particular algorithm. First, the specific problem solved by this algorithm has analogies in many other sectors: The predicted risk of some future outcome (in our case, health care needs) is widely used to target policy interventions under the assumption that the treatment effect is monotonic in that risk, and the methods used to build the algorithm are standard. Mechanisms of bias uncovered in this study likely operate elsewhere. Second, even beyond our particular finding,

# The data

- primary care patients at large academic hospital, “enrolled in risk-based contracts”
- 6079 Black patients, 43,539 White patients self-identified
- **algorithm risk score** for each patient-year 2013–2015
- high-risk patients identified for enrollment into care management program
- algorithm uses several features of each patient in year  $t - 1$ 
  - demographics (not race)
  - insurance type
  - morbidities, medications
  - health system events
  - billed amounts
- to predict health system costs in year  $t$
- health care costs are the “label” (outcome) to identify high-risk subset

- use electronic health records to identify actual events in year  $t$
- create a different outcome variable, **health**  
“total number of chronic illnesses for which patient had a medical encounter in year  $t$ ”
- “of note, ... algorithm developers typically do not have access to [this data] to fit or validate their predictions”
- more detailed analysis using laboratory biomarkers related to common chronic illnesses
- compared results from algorithm using costs, to algorithm using health, in Black and White patients

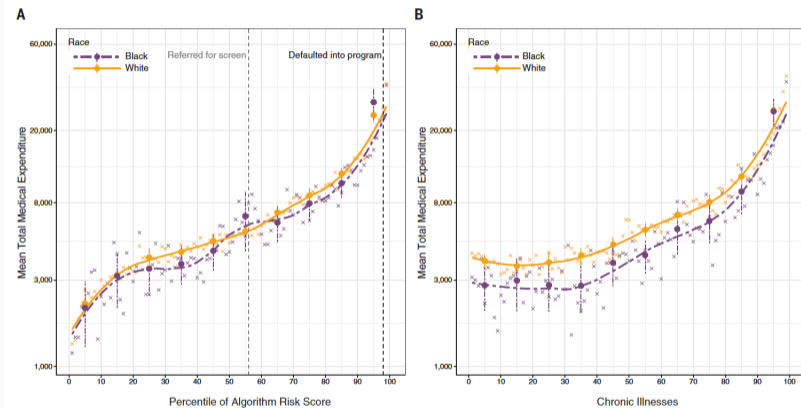
A



- “at the same level of algorithm-predicted risk, Blacks have significantly more illness burden”
- “we find evidence of substantial disparities in program screening”
- why?
- “at a given level of health, Blacks generate lower costs than Whites”
- “As a result, accurate prediction of costs necessarily means being racially biased on health”

“a wedge between **needing** and **receiving** health care”

correlated with race



**Fig. 3. Costs versus algorithm-predicted risk, and costs versus health, by race.** (A) Total medical expenditures by race, conditional on algorithm risk score. The dashed vertical lines show the auto-identification threshold (black line: 97th percentile) and the screening threshold (gray line: 55th percentile). (B) Total medical expenditures by race, conditional on number of chronic conditions. The  $\times$  symbols show risk percentiles; circles show risk deciles with 95% confidence intervals clustered by patient. The y axis uses a log scale.

## The theory

- costs are well-predicted, using covariates related to prior costs, demographics, some health information
- costs are not a good proxy for “health” itself not well-defined
- well-established racial differences in healthcare utilization hence costs
- causal inference, confounding causal diagram
- understanding the data, and the application, bring insight well beyond algorithms

nature portfolio

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## Power and significance: clinical trial benefits with advanced covariate adjustment

Moving from subjective selection of covariates to data-driven methods enhances statistical outcomes, and could bring more drugs through clinical trials to patients.



“Owkin is pioneering HCCNET, an AI and machine learning (ML) approach ... with HCCNET they were able to increase statistical power from 80% to 85%”





# Applications

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**Fun**

NEWS

NEUROSCIENCE

## Americans tend to assume imaginary faces are male

Why people perceive faces in inanimate objects as male by default is still unclear



<sup>2</sup>People often see imaginary faces in everyday objects, such as this smiling face in a cheese grater. These faces were more often seen as male than a new survey.

<sup>3</sup>PAUL DAVID GALVIN/MOMENT/GETTY IMAGES PLUS

PNAS

Proceedings of the  
National Academy of Sciences  
of the United States of America

Institution:  
TORONTO

Keyword, A

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### RESEARCH ARTICLE

## Illusory faces are more likely to be perceived as male than female

 Susan G. Wardle,  Sanika Paranjape,  Jessica Taubert, and  Chris I. Baker

[+ See all authors and affiliations](#)

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## RESEARCH ARTICLE



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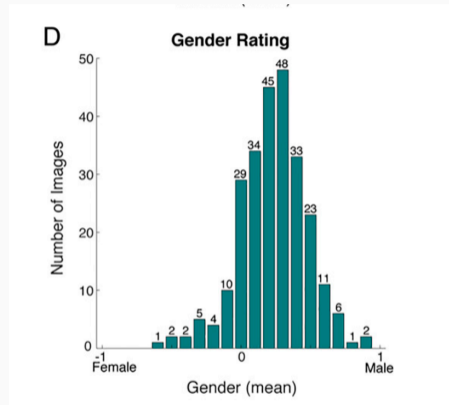
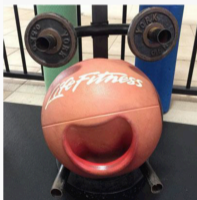
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**Illusory faces are more likely to be perceived as male than female**

Susan G. Wardle, Sanika Paranjape, Jessica Taubert, and Chris I. Baker

[+ See all authors and affiliations](#)

ARTI



<https://osf.io/f74xh/>



OPINION

# Will AI really change everything? Not likely

Although tools like ChatGPT can astonish us with their output, they are not operating anywhere near human intelligence

JOSEPH WILSON

OPINION

PhD candidate in linguistic anthropology at the University of Toronto

Do you have AI fatigue yet? Not a day goes by without breathless commentary on the increasing power of artificial-intelligence models. A deluge of new apps and services promises to disrupt everything from health care to education. “The future is here,” we are told. “Are you ready?”

blindly optimistic, claiming that AI will magically solve everything from climate change to the opioid crisis, or they are darkly dystopian, warning us that AI could escape its silicon chains and destroy humanity.

Even when AI developers themselves “warn” people of the existential threats AI could pose, as they did in an open letter recently calling for a pause in development, it functions as a marketing campaign. The tech companies are essentially congratulating each other for creating something too good. Google’s chief executive, Sundar Pichai, has called AI, without irony, a technology “more profound than fire or electricity.”

The public doesn’t know what to believe and they’re worried. A newly released poll conducted by Innovative Research Group for the 2023 Provocation Ideas Festival shows that 47 per cent of Canadians are more concerned than excited about the increased

“future-proof your career” or “become AI literate.”

The reality is that most of what we read about AI is hype. In the near term, this new crop of AI tools will probably give us slightly better-written spam in our inboxes and reams of crappy, machine-generated websites. Real, life-saving applications are indeed possible in fields such as health care and agriculture, but they’ll be hard to spot amid all the junk. Although tools such as ChatGPT and Midjourney are fun to play with and can astonish us with their output, they are not operating anywhere near human intelligence. They are essentially performing a clever parlour trick.

The reason we are astonished by their output is because, as a species, we’re gullible. We tend to read human characteristics into any pattern that even mildly resembles a human. We see faces in electrical sockets and spot human silhouettes in evening shadows. We feel bad for a discarded

heightened empathy is one of the ways technology companies have captured the public’s attention in recent months. OpenAI launched ChatGPT (which generates text) and DALL-E (which generates images) online and for free so the public could play around with them. It let the public work itself into a frenzy as they identified characteristics in the programs that were previously thought to be exclusively human: reason, humour, emotion, creativity. But generative AI can do none of these things. It has the form of human expression but no content.

The technology that runs under the hood of these tools is not fundamentally new. The mathematical models have changed in recent years, and new chips are making computation cheaper and more efficient, but ChatGPT only functions like a powerful autocomplete feature. Trained on an enormous amount of data, the model predicts which words

sky-high, further concentrating capital and technological knowledge in the hands of very few billionaires. As such, the field of AI is desperately in need of regulation. This is necessary not because tech companies might unleash a mathematical model that will suddenly become conscious and take over the world, but for the very real, boring reasons that have always existed: so they don’t take advantage of poorly paid temp workers, or refuse calls to be transparent with their algorithms, or flood social media with misinformation, or violate copyright laws by scraping the web for data without the permission of its owners. Sadly, these are things that Big Tech is already doing, and governments have been slow to act.

Fear, as populist politicians and headline writers know well, is best evoked by appealing to the unknown. Whether it’s the fear of AI-gone-rogue or the fear of falling behind in the race to

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## **Back to Theory**

---

1. **Drought** Climate change attribution  
climate models, subgroup analyses, predictions
2. **Covid** Treatment with Ivermectin  
randomized trial, proportional hazards regression, Bayes/frequentist
3. **Health Care** Algorithmic bias  
choice of outcome variable, confounding, visualization
4. **Faces** Human perception  
sign test, regression, computational modelling



- statistical “workflows” seem to be emerging in different disciplines
  - Drought — “A Protocol for probabilistic extreme event attribution analysis ”  
Philip et al 2020, *Adv. Stat. Clim. Met. Ocean*
  - “Writing statistical methods for ecologists” Davis & Kay 2023, *Ecosphere*
- tutorial-type articles in scientific journals
  - *Annals of Thoracic Surgery* — the statistician’s page
  - *J Am Medical Association* — Guide to Statistics and Methods
  - *Nature Methods* — Points of Significance
- “open data” continues to be elusive
  - Drought — “Almost all the data are available via the KNMI Climate Explorer”
  - Covid — “... the data will be made publicly available”
  - Healthcare — [synthetic data and code posted online](#)
  - Faces — [pictures available](#), data less clear

# Communication!

June 5, 2023



**SIGMA XI**  
THE SCIENTIFIC SOCIETY OF AMERICAN PHYSICISTS

Original URL:  
<https://smartbrief.com/news/2023/06/05/US-life-expectancy-declining-for-decades/>

Click to follow link.

## SmartBrief

Your World of Science News

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### Study predicts extreme precipitation to increase by 52%

Precipitation events that deliver heavy rainfall or melted snowfall in one day are predicted to increase 52% in the Northeast by the end of the century, according to a study in Climatic Change. There will be a large increase in the number of days with extreme rain or snow, researchers predict, and a smaller increase in the amount of precipitation during each event, with extreme precipitation expected to happen mostly in winter and spring. **Full Story:** [New Hampshire Public Radio](#) (6/5)



### Human Cell Atlas project reveals new information about cellular function

Researchers working on the Human Cell Atlas project are learning more about how the placenta, immune system, brain, lungs and other organs function, and they have discovered thousands of new types of cells using single-cell genomics and advanced computational technology. The researchers have discovered how placental cells interact and function, identified a previously unknown lung cell type involved in cystic fibrosis, and identified two sets of nasal cells SARS-CoV-2 uses to infect people. **Full Story:** [The Guardian \(London\)](#) (6/3)

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### US life expectancy has been declining for decades

A report in the American Journal of Public Health found US life expectancy has been steadily declining since the 1950s, and the COVID-19 pandemic further widened the gap between the US and other high-income nations as the US recorded more deaths from the

“US Life expectancy has been declining for decades”

June 5, 2023



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### Falling Behind: The Growing Gap in Life Expectancy Between the United States and Other Countries, 1933–2021

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#### Abstract

**Objectives.** To document the evolution of the US life expectancy disadvantage and regional variation across the US states.

**Methods.** I obtained life expectancy estimates in 2022 from the United Nations, the Human Mortality Database, and the US Mortality Database, and calculated changes in growth rates, US global position (rank), and state-level trends.

**Results.** Increases in US life expectancy slowed from 1950 to 1954 (0.21 years/annum) and 1955 to 1973 (0.10 years/annum), accelerated from 1974 to 1982 (0.34 years/annum), and progressively deteriorated from 1983 to 2009 (0.15 years/annum), 2010 to 2019 (0.06 years/annum), and 2020 to 2021 (−0.97 years/annum). Other countries experienced faster growth in each phase except 1974 to 1982. During 1933 to 2021, 56 countries on 6 continents surpassed US life expectancy. Growth in US life expectancy was slowest in Midwest and South Central states.

**Conclusions.** The US life expectancy disadvantage began in the 1950s and has steadily worsened over the past 4 decades. Dozens of globally diverse countries have outperformed the United States. Causal factors appear to have been concentrated in the Midwest and South.

June 5, 2023



**SIGMA XI**  
THE SCIENTIFIC SOCIETY OF WOMEN

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<https://smartbrief.com/news/2023/06/05/Study-Predicts-Extreme-Precipitation-Increase-52%/>

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## Study predicts extreme precipitation to increase by 52%

Precipitation events that deliver heavy rainfall or melted snowfall in one day are predicted to increase 52% in the Northeast by the end of the century, according to a study in Climatic Change. There will be a large increase in the number of days with extreme rain or snow, researchers predict, and a smaller increase in the amount of precipitation during each event, with extreme precipitation expected to happen mostly in winter and spring. **Full Story:** [New Hampshire Public Radio](#) (6/5)



## Human Cell Atlas project reveals new information about cellular function

Researchers working on the Human Cell Atlas project are learning more about how the placenta, immune system, brain, lungs and other organs function, and they have discovered thousands of new types of cells using single-cell genomics and advanced computational technology. The researchers have discovered how placental cells interact and function, identified a previously unknown lung cell type involved in cystic fibrosis, and identified two sets of nasal cells SARS-CoV-2 uses to infect people. **Full Story:** [The Guardian \(London\)](#) (6/3)



## US life expectancy has been declining for decades

A report in the American Journal of Public Health found US life expectancy has been steadily declining since the 1950s, and the COVID-19 pandemic further widened the gap between the US and other high-income nations as the US recorded more deaths from the



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## Falling Behind: The Growing Gap in Life Expectancy Between the United States and Other Countries, 1933–2021

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### Abstract

**Objectives.** To document the evolution of the US life expectancy disadvantage and regional variation across the US states.

**Methods.** I obtained life expectancy estimates in 2022 from the United Nations, the Human Mortality Database, and the US Mortality Database, and calculated changes in growth rates, US global position (rank), and state-level trends.

**Results.** Increases in US life expectancy slowed from 1950 to 1954 (0.21 years/annum) and 1955 to 1973 (0.10 years/annum), accelerated from 1974 to 1982 (0.34 years/annum), and progressively deteriorated from 1983 to 2009 (0.15 years/annum), 2010 to 2019 (0.06 years/annum), and 2020 to

“Increases in US life expectancy slowed”

# Science

PERSPECTIVE | HEALTH

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July 21, 2023

## Heart failure causes sleepless nights

Cardiac dysfunction triggers immune-mediated loss of pineal gland melatonin release

By Harvey Davis and David Attwell

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RESEARCH ARTICLE | HEART DISEASE



## Immune-mediated denervation of the pineal gland underlies sleep disturbance in cardiac disease

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SCIENCE · 20 Jul 2023 · Vol 381, Issue 6655 · pp. 285-290 · DOI:10.1126/science.abn6366

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In mice  
and in cells



# Science



## Trust shapes views on science

**PUBLIC OPINION** | Just 51% of Americans who express low trust in government and other institutions are fully vaccinated for COVID-19 versus 89% with high institutional trust, a survey has found. Although Republican respondents expressed less of this trust than Democrats overall, individuals with high trust were more likely to get vaccinated than those with low trust even within each party, according to results from the online survey, released last week by the right-leaning American Enterprise Institute. Overall, trust in scientists fell during the pandemic: Only 69% of the 5055 respondents expressed confidence that scientists would act in the public's best interests, down from 86% in January 2019.



## America's Crisis of Confidence: Rising Mistrust, Conspiracies, and Vaccine Hesitancy After COVID-19

September 28, 2023 | Daniel A. Cox, M. Anthony Mills, Ian R. Banks, Kelsey Eyre Hammond, Kyle Gray



- probability, analysis, applied mathematics modelling
- Bayes, Neyman, Fisher approaches to inference
- nature of uncertainty epistemic, empirical
- nature of induction belief functions, inferential models
- interpretation of  $p$ -values, confidence regions, credibility intervals, likelihood ratios
- role of sufficiency, ancillarity, conditioning, asymptotic theory
- sparsity, causality, assumption-free/lean inference, stability, prediction

## ... Back to foundations

- probability, analysis, applied mathematics modelling
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- nature of induction belief functions, inferential models
- interpretation of  $p$ -values, confidence regions, credibility intervals, likelihood ratios
- realistic estimates of precision, complex dependencies, subgroup analyses
- sparsity, causality, assumption-free/lean inference, stability, prediction

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