

28 novembre 2025

14<sup>ème</sup> Forum Cancéropôle Est

Besançon

ENSEMBLE, PRENONS  
LE CANCER DE VITESSE

## L'Intelligence artificielle: une nouvelle arme contre le cancer

*Nature, 2020*

# L'IA, promesse ou menace ?

2



## What Humans Lose When We Let AI Decide

Why you should start worrying about artificial intelligence now:

Christine Moore, Frank van Houdt, and Dirk Lindemann • February 17, 2022 READING TIME: 9 MIN

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## Une brève histoire de l'IA

### Définitions et concepts

### Applications en cancérologie

### Challenges et Perspectives

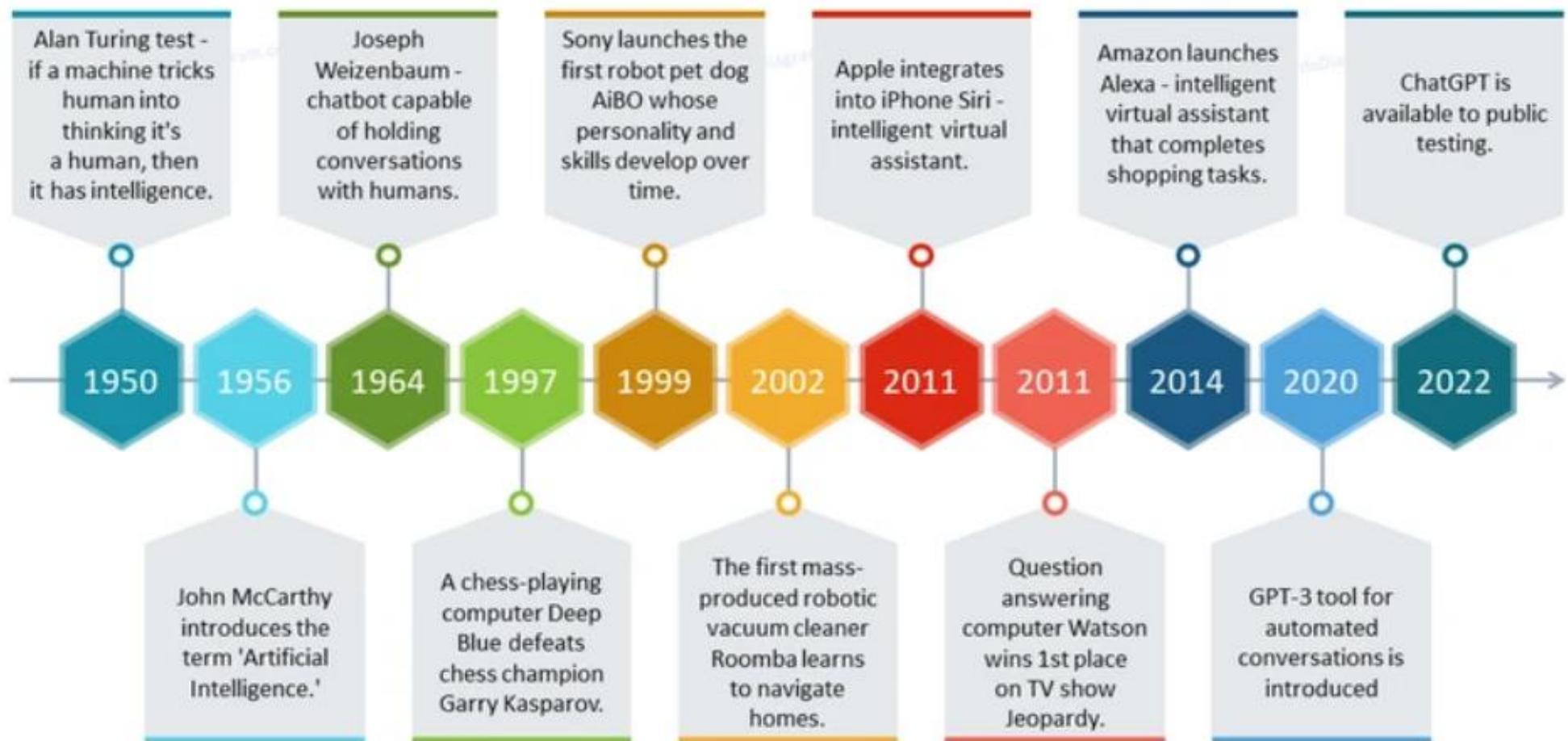


Science & société Tendance

### Intelligence artificielle : elle veut faire parler nos morts

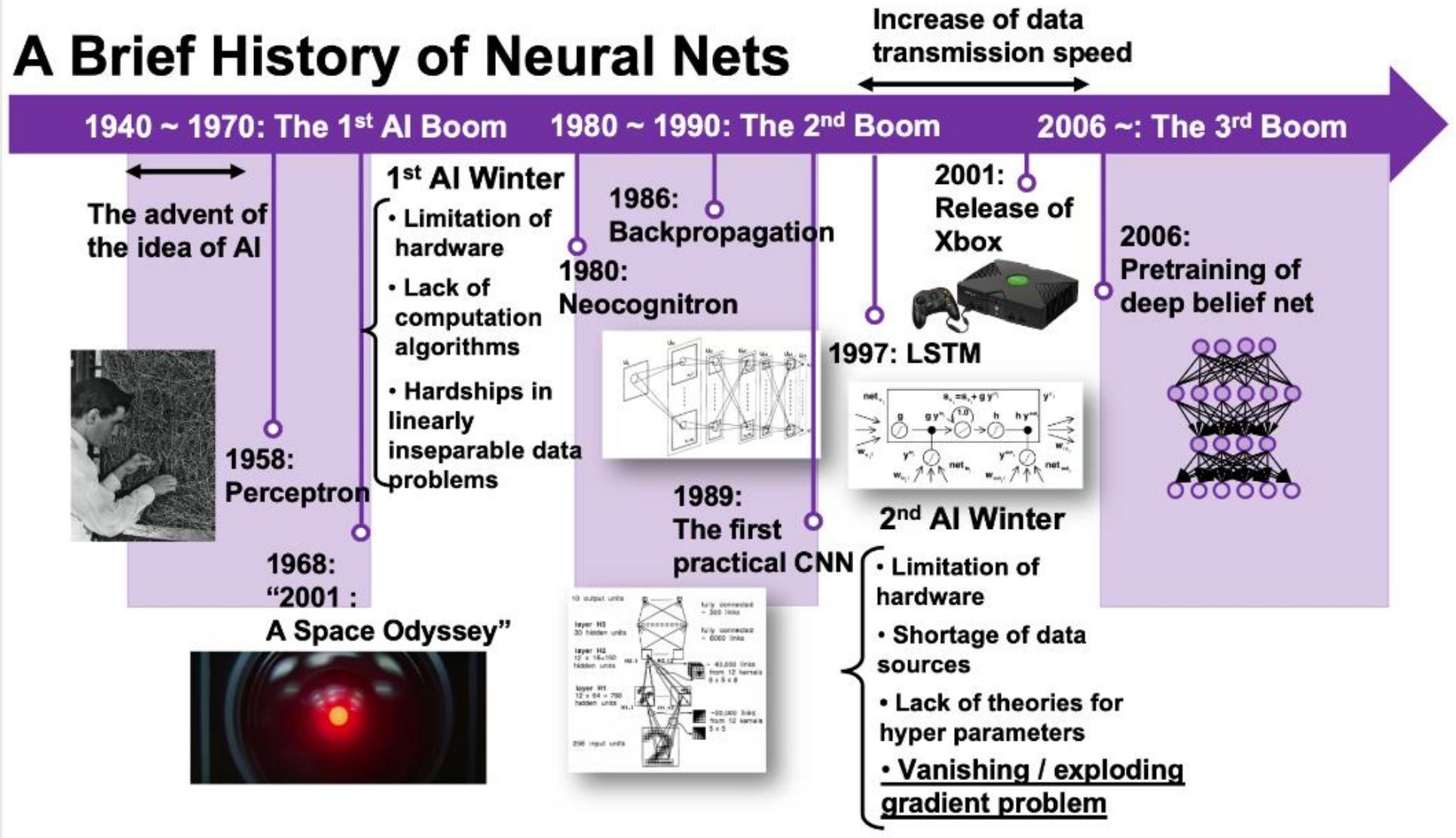


## Artificial Intelligence Development History Timeline

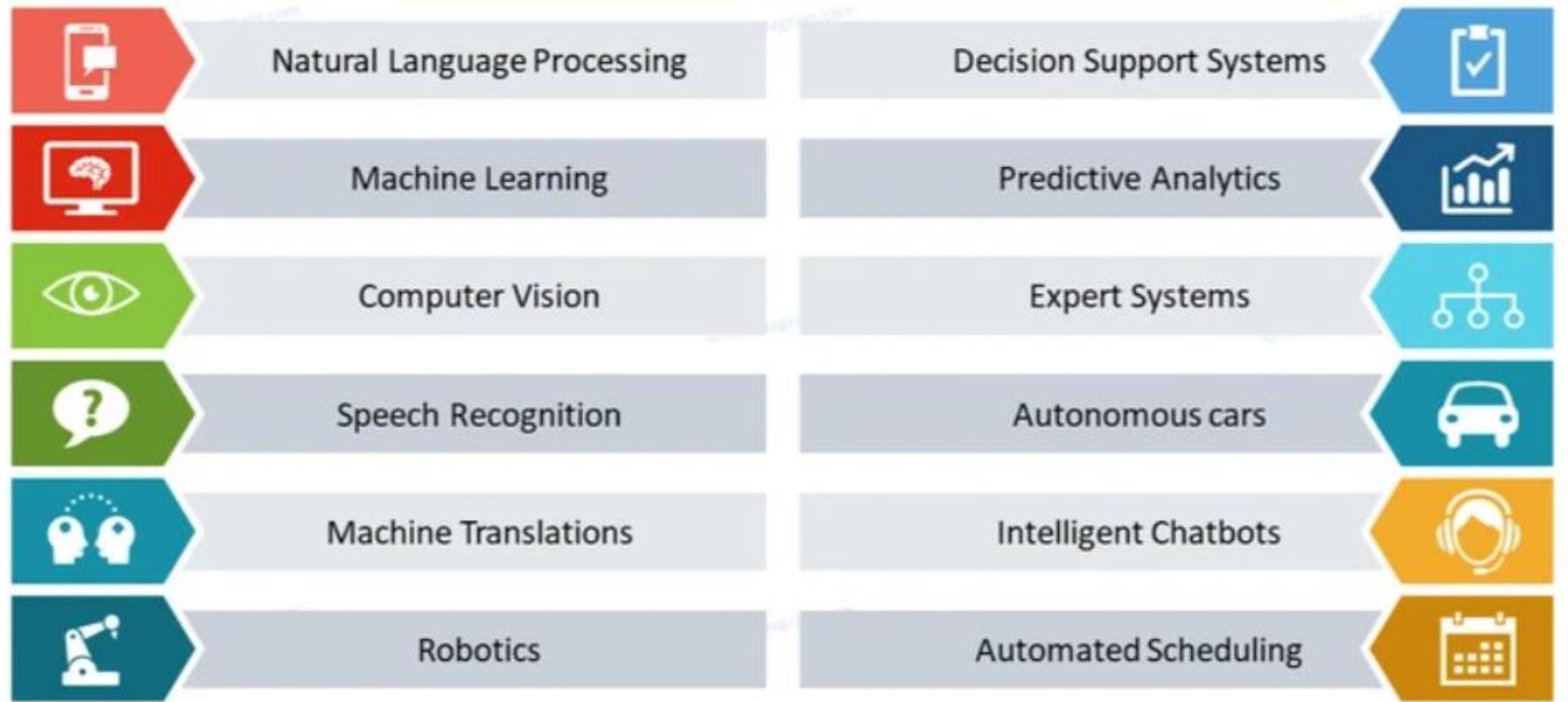


infodiagram.com

## A Brief History of Neural Nets



<https://data-science-blog.com/blog/2020/07/16/a-brief-history-of-neural-nets-everything-you-should-know-before-learning-lstm/>



# 3 Key Artificial Intelligence Statistics You Should Know



## 1 Which processes rely heavily on AI?

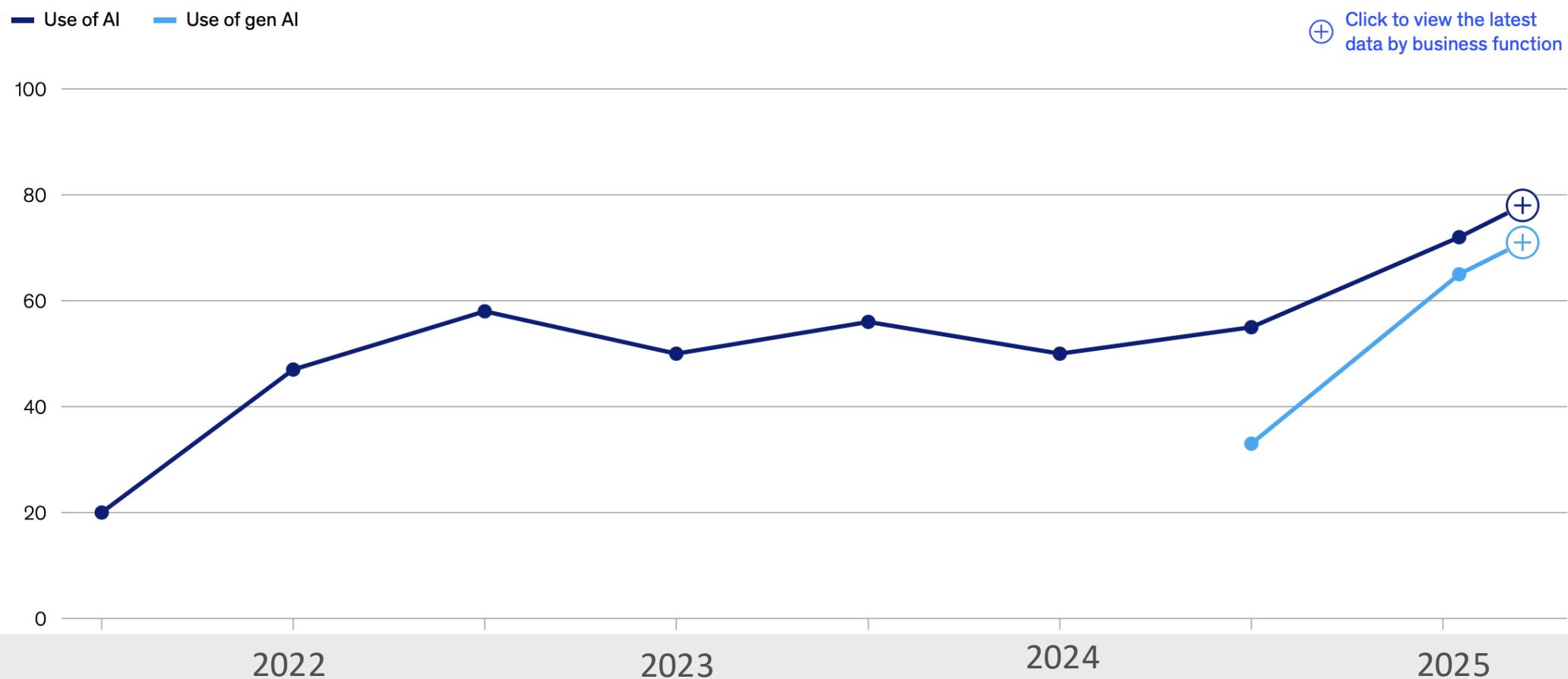
Source: Statista

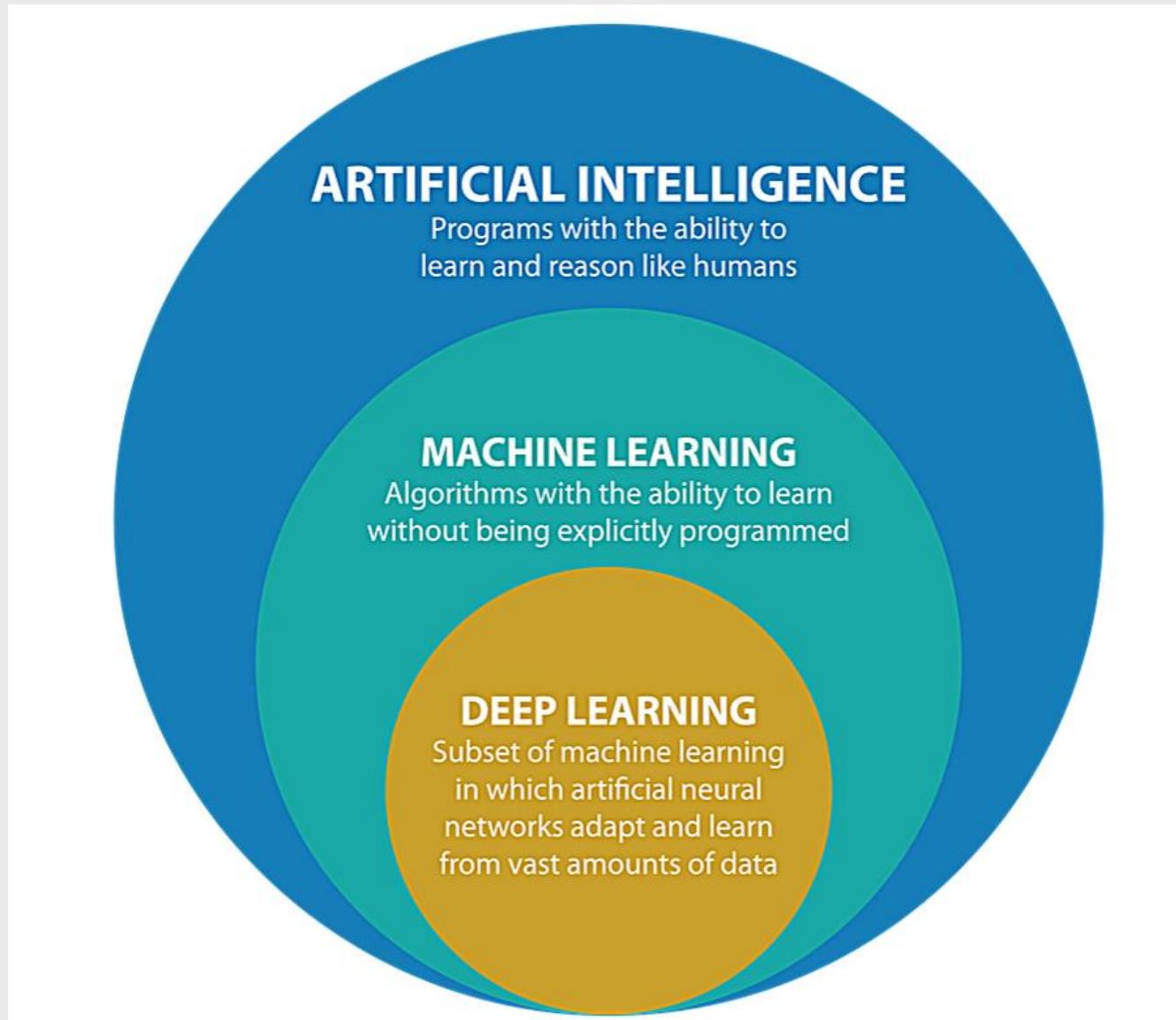
Global AI ranked by revenue of use cases:



## Organizations' use of AI has accelerated markedly in the past year, after years of little meaningful change.

Organizations that use AI in at least 1 business function,<sup>1</sup> % of respondents

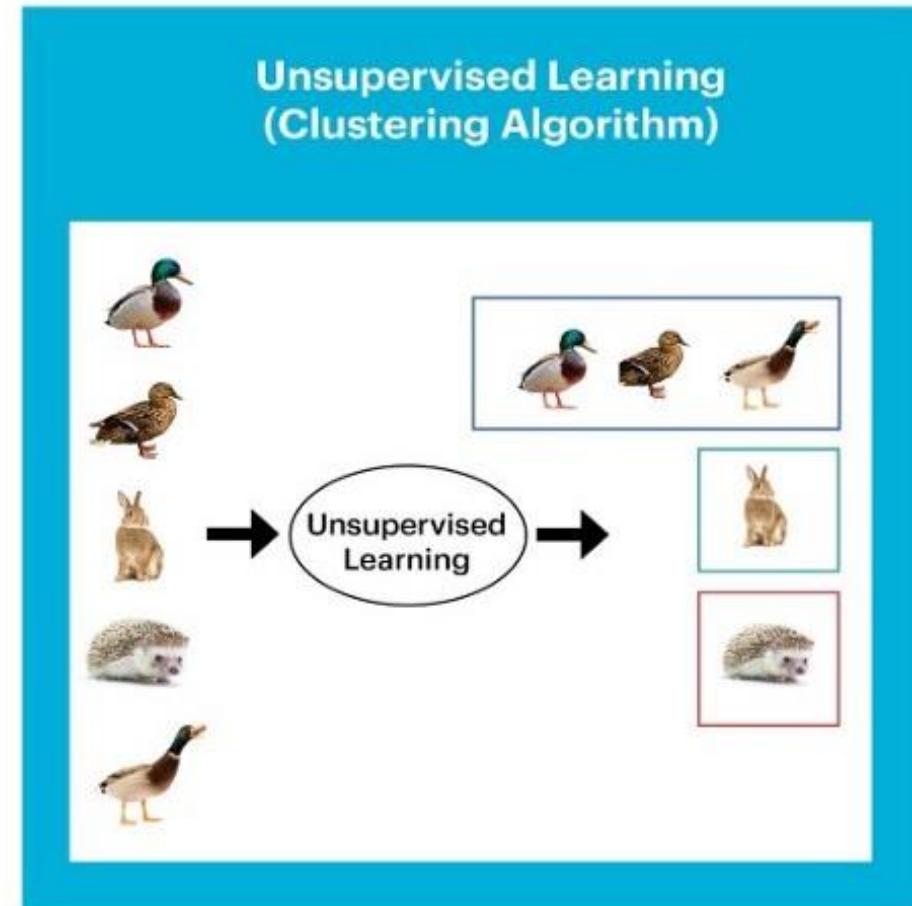
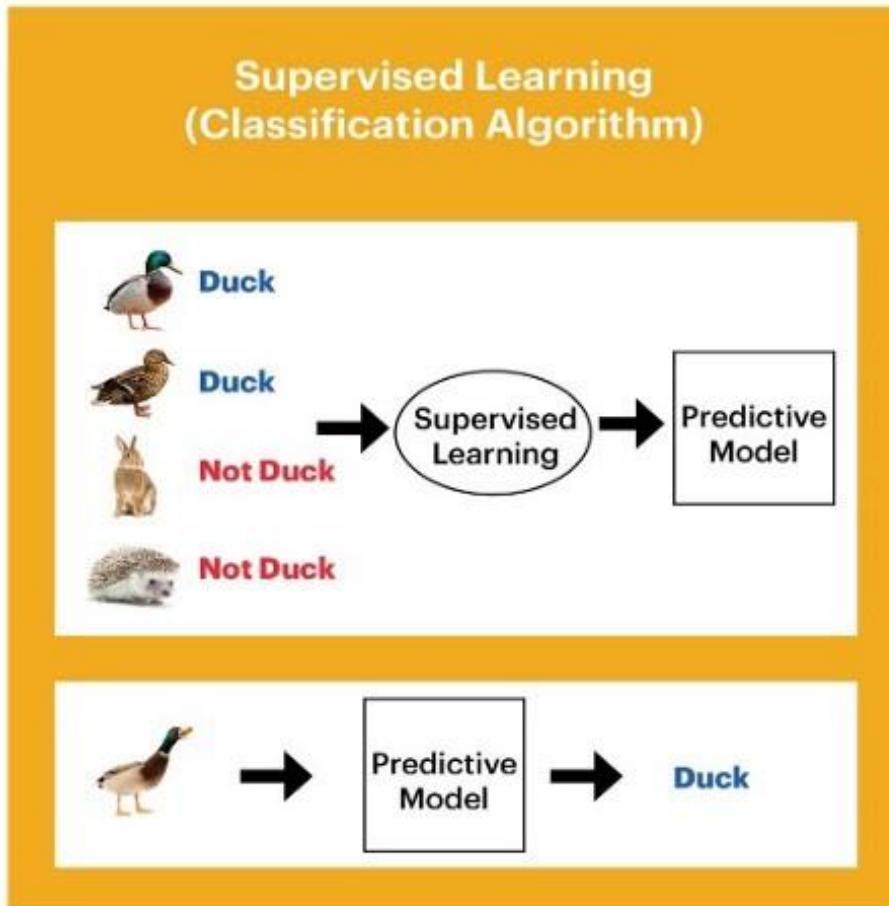




<https://blog.digitalogy.co/the-difference-between-artificial-intelligence-machine-learning-and-deep-learning/>

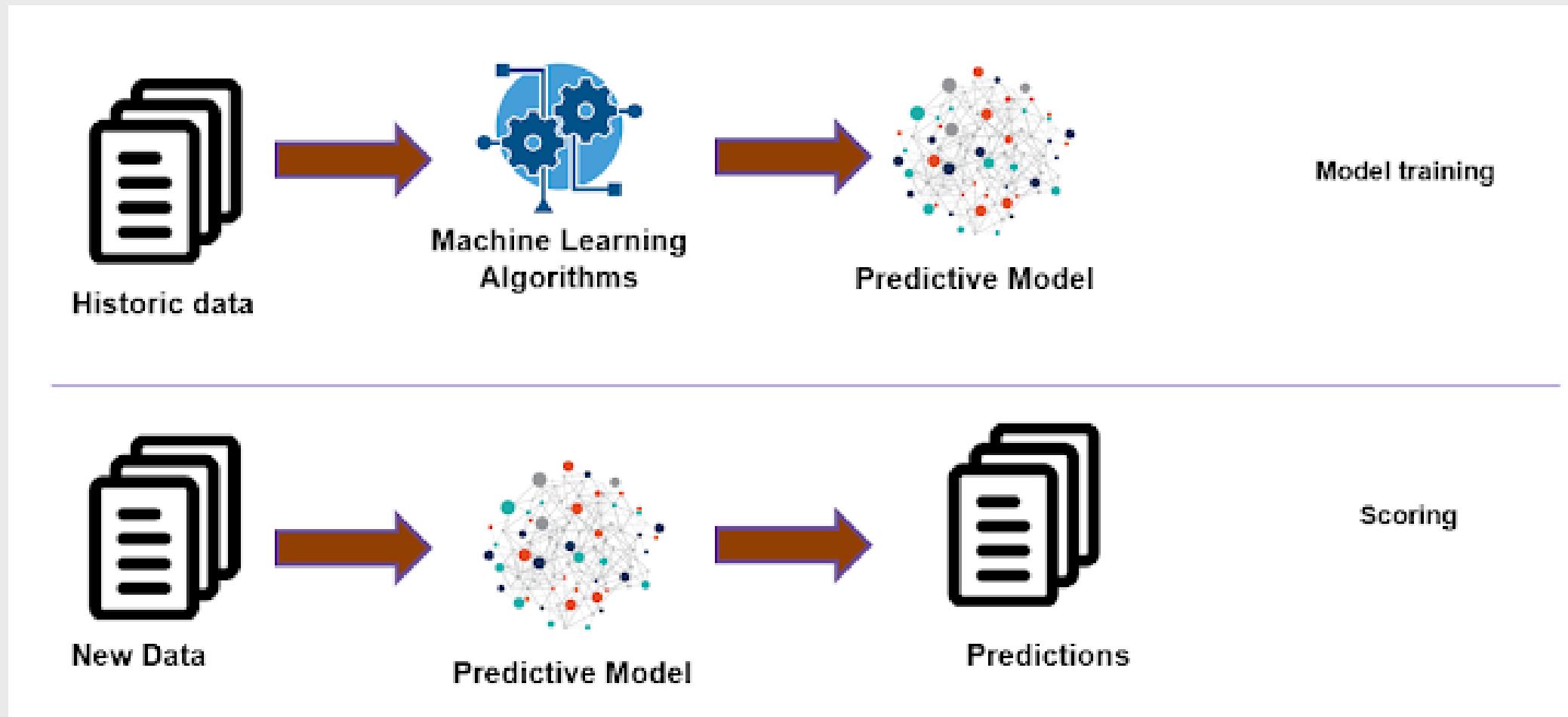
# Principales définitions et modèles

9



Western Digital.

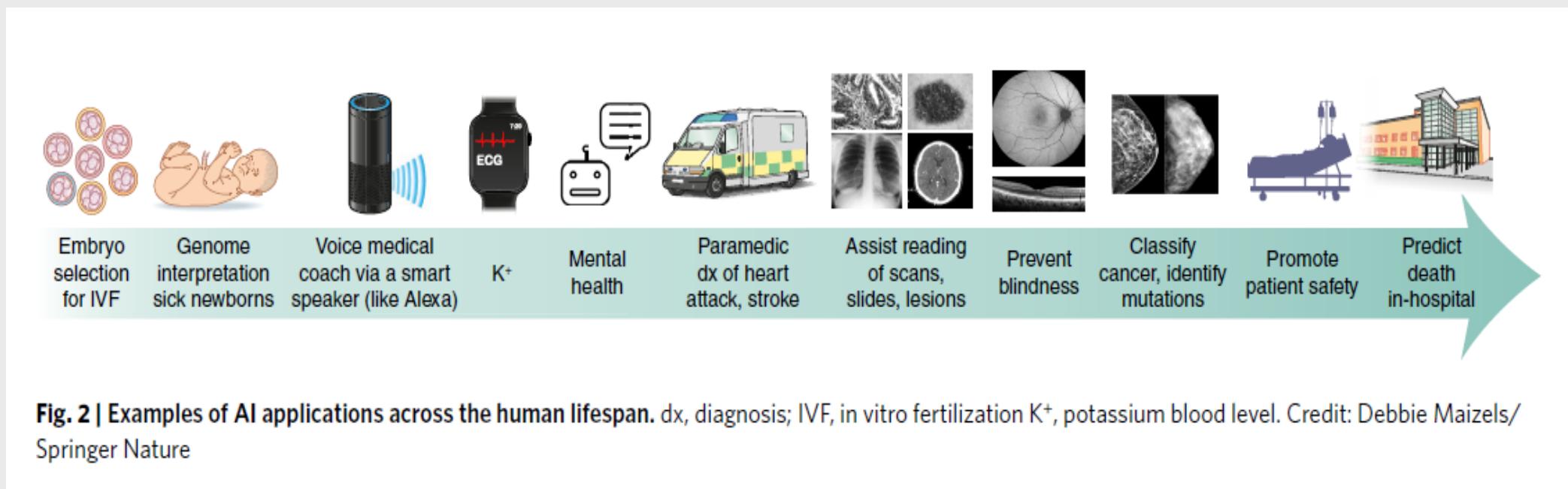
<https://laptrinhx.com/supervised-vs-unsupervised-learning-1861950659/>



<http://singaporebusinessintelligence.blogspot.com/2018/10/what-is-automated-machine-learning.html>

# Quelques applications potentielles de l'IA en médecine

11



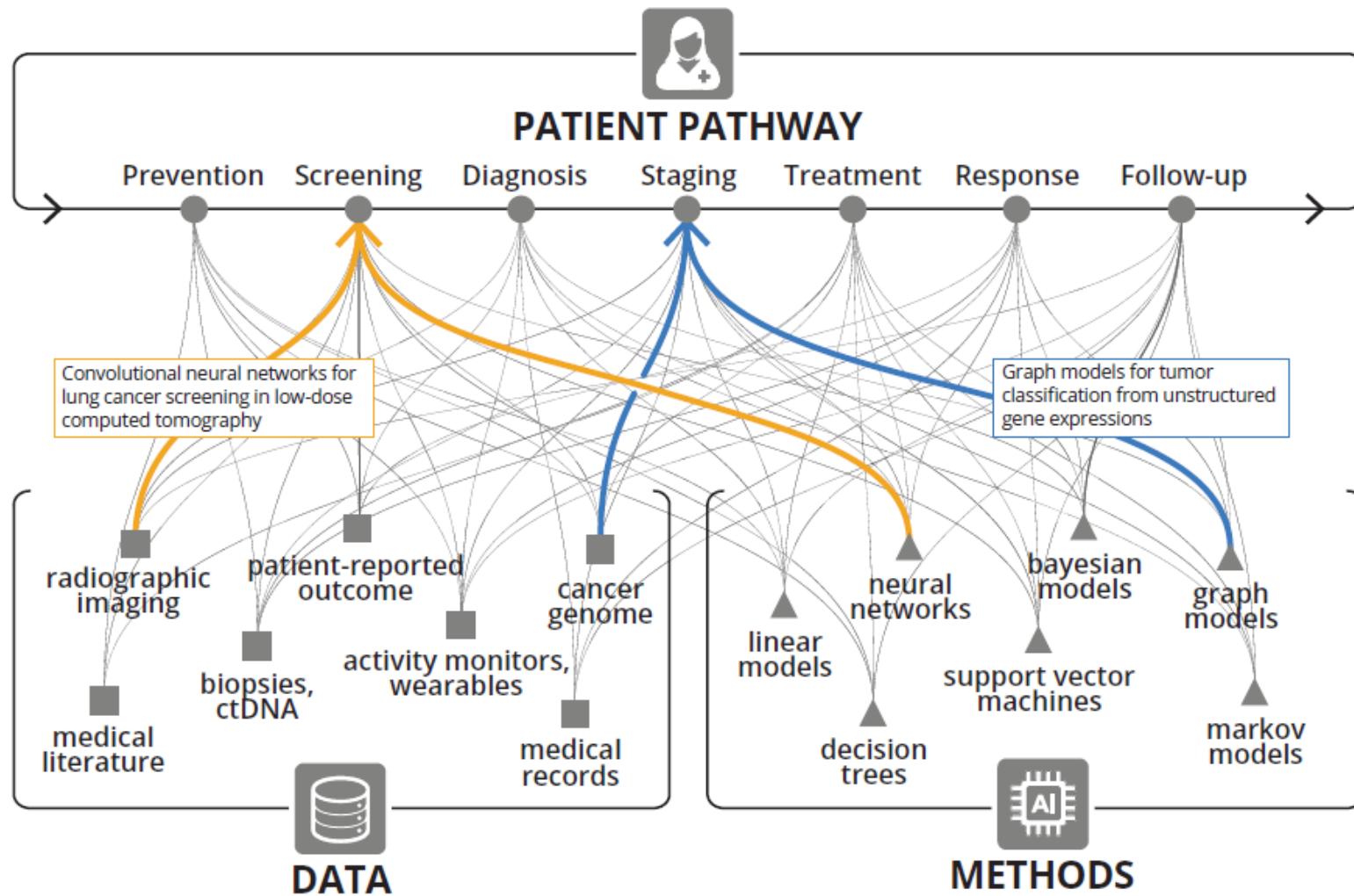
**Fig. 2 | Examples of AI applications across the human lifespan.** dx, diagnosis; IVF, in vitro fertilization K<sup>+</sup>, potassium blood level. Credit: Debbie Maizels/ Springer Nature

Topol, Nat Med 2019

- IA capable de générer du « nouveau contenu »
- ... à partir de ce qu'elle a appris!
- Texte, images, sons, vidéos,...
- IA non-supervisée
  - Réseaux antagonistes de neurones (GAN)
  - GPT (Generative Pretrained Transformer)
- Applications en médecine
  - Conseils
  - Téléconsultations
  - ...
- Mêmes biais que l'IA non générative!



MED-PALM2: ChatGPT médical de Google



Kann, *Cancer Cell* 2021

## LETTER

doi:10.1038/nature21056

### Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva<sup>1\*</sup>, Brett Kuprel<sup>1\*</sup>, Roberto A. Novoa<sup>2,3</sup>, Justin Ko<sup>2</sup>, Susan M. Swetter<sup>2,4</sup>, Helen M. Blau<sup>5</sup> & Sebastian Thrun<sup>6</sup>

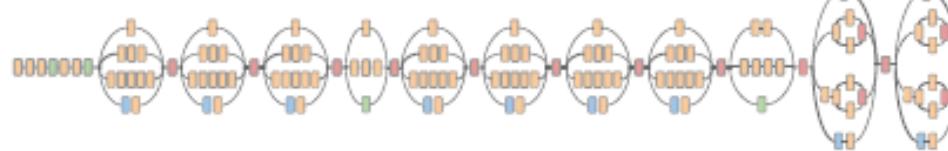
Nature 2017

Training dataset: 129 450 images, 757 maladies

Skin lesion image



Deep convolutional neural network (Inception v3)



- Convolution
- AvgPool
- MaxPool
- Concat
- Dropout
- Fully connected
- Softmax

Training classes (757)

- Acral-lentiginous melanoma
- Amelanotic melanoma
- Lentigo melanoma
- ...
- Blue nevus
- Halo nevus
- Mongolian spot
- ...
- ...
- ...

Inference classes (varies by task)

- 92% malignant melanocytic lesion
- 8% benign melanocytic lesion

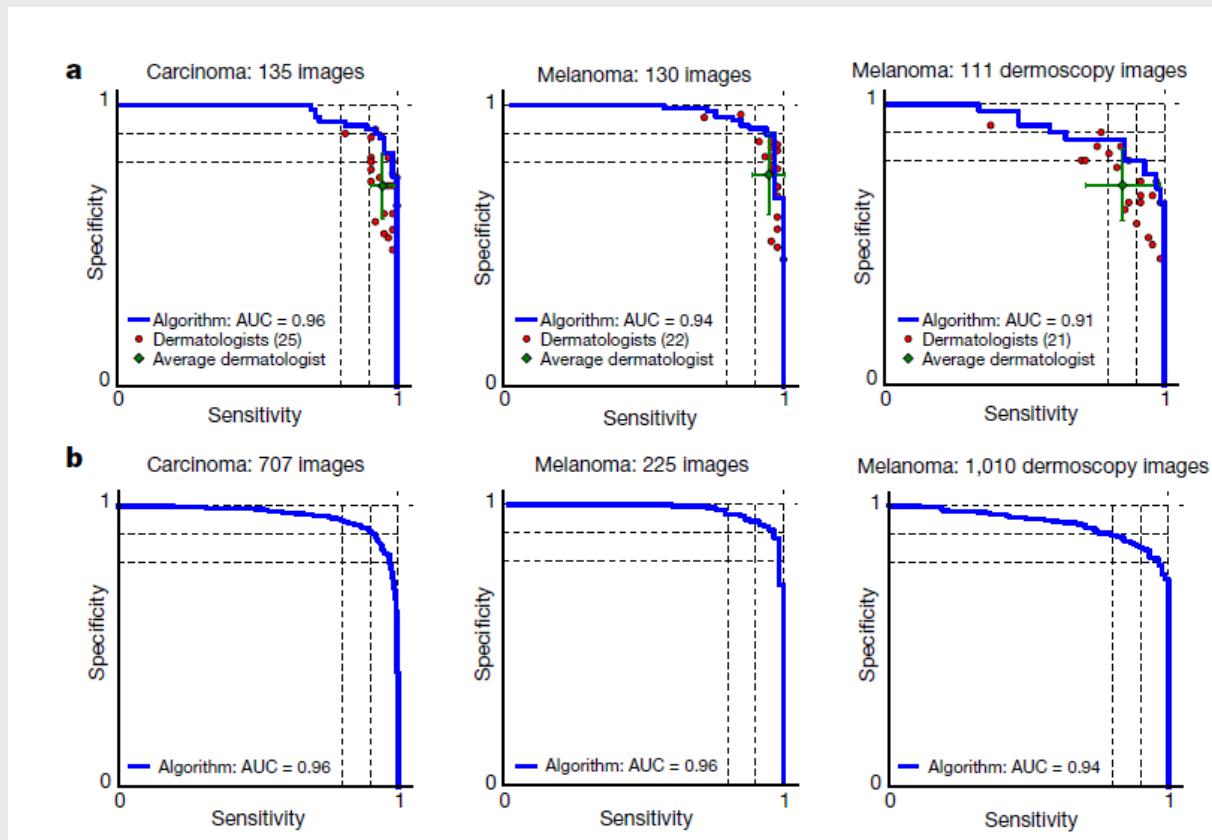
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Test dataset  
Comparaison algorithme vs 21 dermatologues



# IA à visée diagnostique: radiologie

## Training dataset:

mammographies de 25 856 femmes (UK)

## Test dataset:

mammographies de 3097 femmes (US)

## Article

# International evaluation of an AI system for breast cancer screening

<https://doi.org/10.1038/s41586-019-1799-6>

Received: 27 July 2019

Accepted: 5 November 2019

Published online: 1 January 2020

Scott Mayer McKinney<sup>1,14\*</sup>, Marcin Sieniek<sup>1,14</sup>, Varun Godbole<sup>1,14</sup>, Jonathan Godwin<sup>2,14</sup>, Natasha Antropova<sup>2</sup>, Hutan Ashrafiyan<sup>3,4</sup>, Trevor Back<sup>2</sup>, Mary Chesus<sup>2</sup>, Greg S. Corrado<sup>1</sup>, Ara Darzi<sup>3,4,5</sup>, Mozziyar Etemadi<sup>6</sup>, Florencia Garcia-Vicente<sup>6</sup>, Fiona J. Gilbert<sup>7</sup>, Mark Halling-Brown<sup>8</sup>, Demis Hassabis<sup>9</sup>, Sunny Jansen<sup>9</sup>, Alan Karthikesalingam<sup>10</sup>, Christopher J. Kelly<sup>10</sup>, Dominic King<sup>10</sup>, Joseph R. Ledsam<sup>2</sup>, David Melnick<sup>6</sup>, Hormuz Mostofi<sup>1</sup>, Lily Peng<sup>1</sup>, Joshua Jay Reicher<sup>11</sup>, Bernardino Romera-Paredes<sup>2</sup>, Richard Sidebottom<sup>12,13</sup>, Mustafa Suleyman<sup>2</sup>, Daniel Tse<sup>14</sup>, Kenneth C. Young<sup>8</sup>, Jeffrey De Fauw<sup>2,15</sup> & Shravya Shetty<sup>1,15\*</sup>

Nature 2020

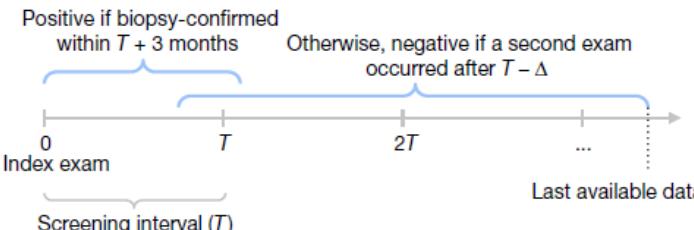
## Test datasets



Number of women	25,856	3,097
Interpretation	Double reading	Single reading
Screening interval	3 years	1 or 2 years
Cancer follow-up	39 months	27 months
Number of cancers	414 (1.6%)	686 (22.2%)

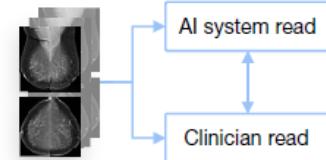


## Ground-truth determination



## Evaluation

Comparison with retrospective clinical performance

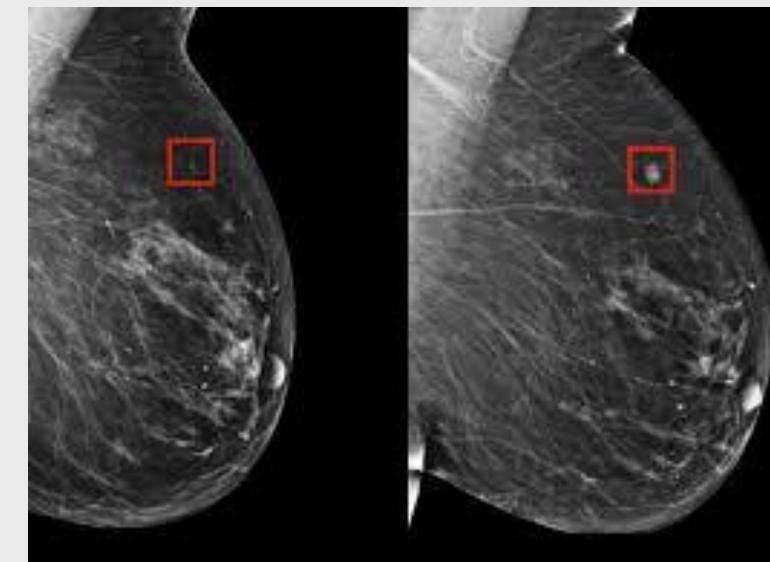
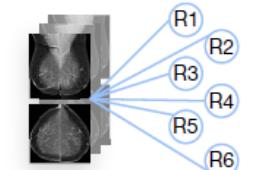


UK and US test sets

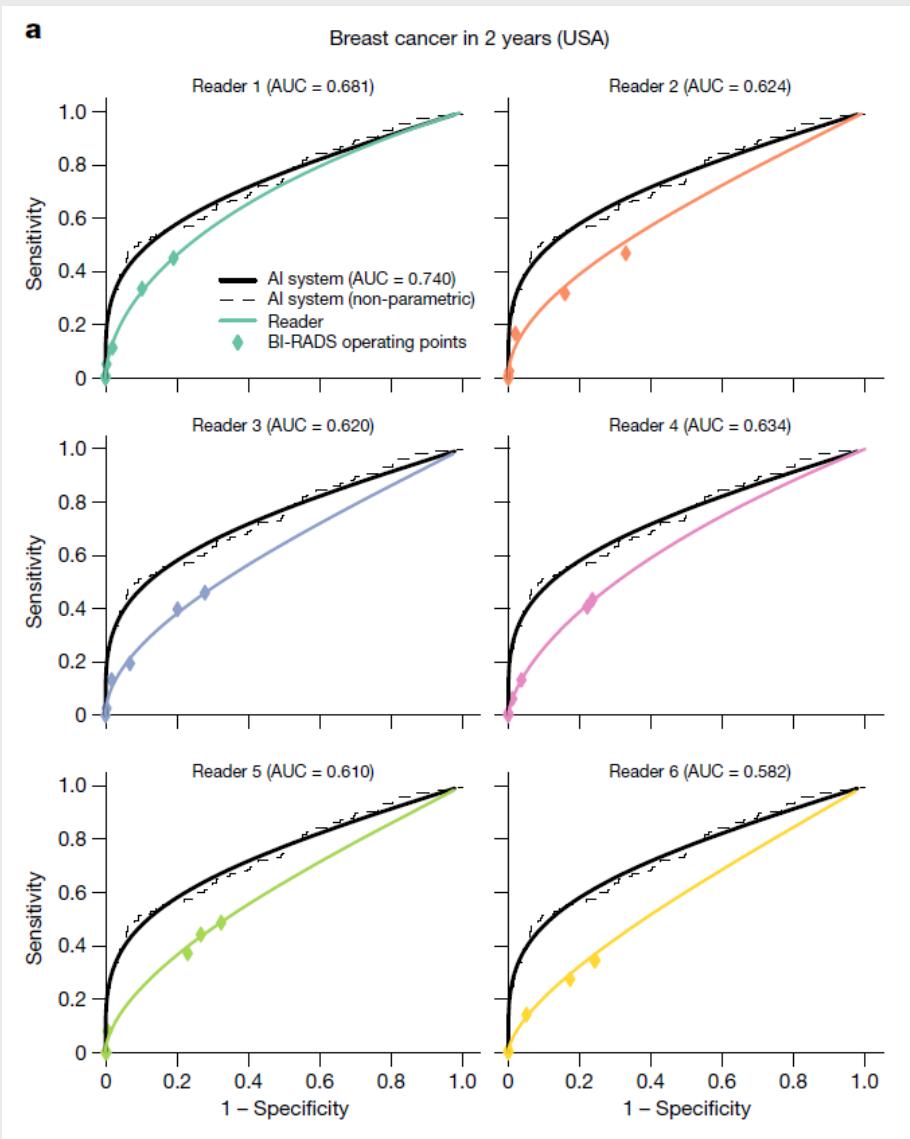
Generalization across datasets



Independently conducted reader study



# IA à visée diagnostique: radiologie



## Article

# International evaluation of an AI system for breast cancer screening

<https://doi.org/10.1038/s41586-019-1799-6>

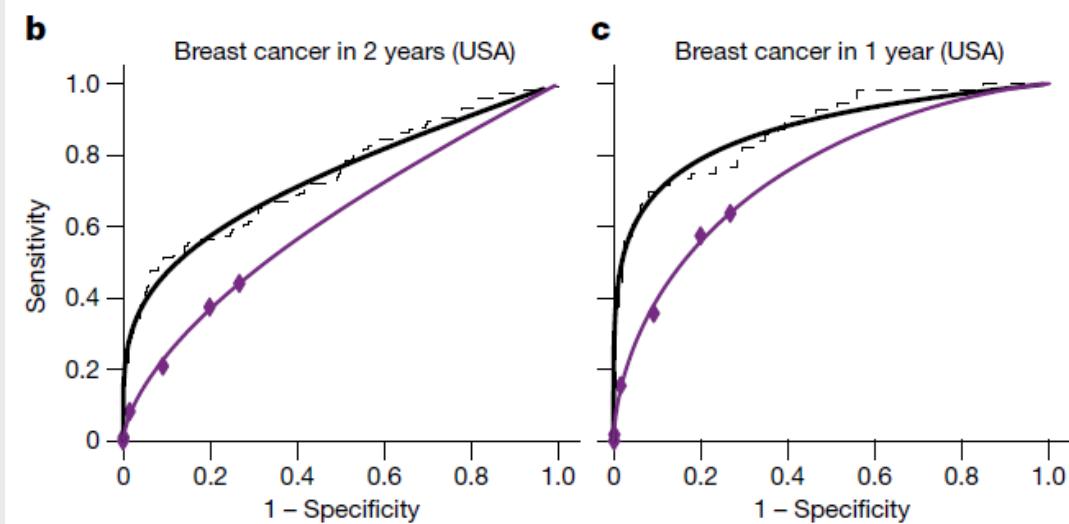
Received: 27 July 2019

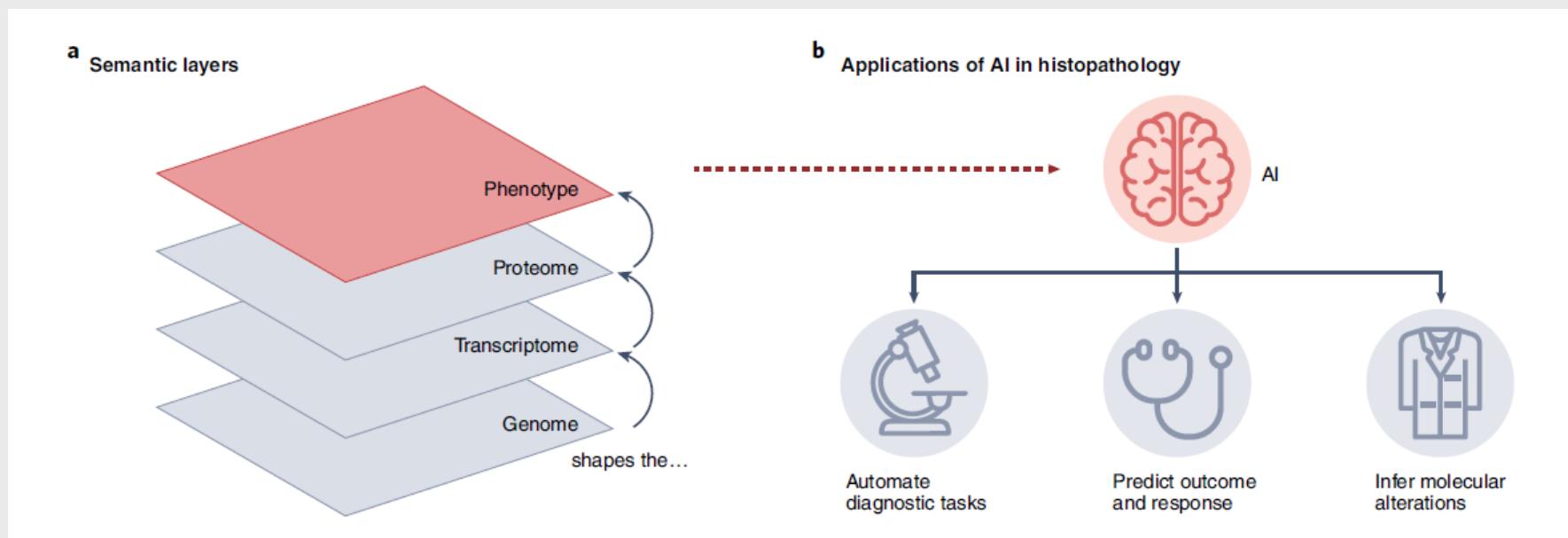
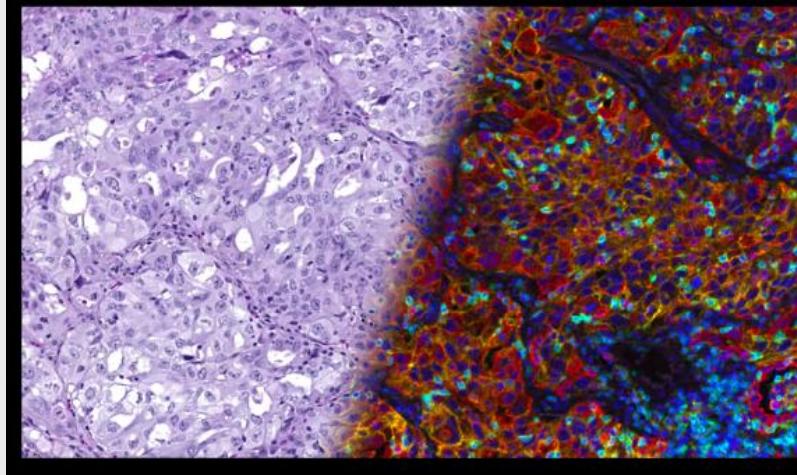
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Comparaison aux performances de 6 radiologues indépendants sur 500 examens





Shmatko, *Nature Cancer* 2022

Type de donnée	Exemple de prédition
Séquence ADN	Accessibilité du génome Organisation 3D du génome Bénéfice d'un traitement
Gènes exprimés (ARN)	Régulation transcriptionnelle Modules de co-expression Classification diagnostique
Séquence protéique	Fonction de la protéine Interactions protéiques
Structure moléculaire	Activité anti-cancéreuse Toxicité Génération de nouvelles molécules
Réseau d'interactions protéiques	Effets secondaires

Greener, *Nature Review Molecular Cell Biology* 2021

Homme de 32 ans

Métastases osseuses et ganglionnaire de primitif inconnu

#### Microscopie

En microscopie, matériel tumoral peu différencié en travées et nappes de cellules cohésives, avec un foyer unique de formation acineuse en bordure de prélèvement. Les cellules ont un cytoplasme par endroit légèrement clarifié.

#### Immunohistochimie:

CKAE1/AE3, CK8/18, EMA : marquage intense des cellules tumorales, hétérogène, d'environ 70% des cellules.

CK19 : marquage de rares cellules tumorales

CK7, p40, PSA, HepPAR1, TTF1, CDX2, pS100, CK20, HER2, SALL4, CD56, Synaptophysine, Chromogranine A, CD3, CD20, CD79a : absence de marquage

CD10 : marquage hétérogène d'une partie des cellules tumorales

PAX8 : marquage nucléaire intense de la majorité des cellules tumorales

Racémase: marquage d'une partie des cellules tumorales

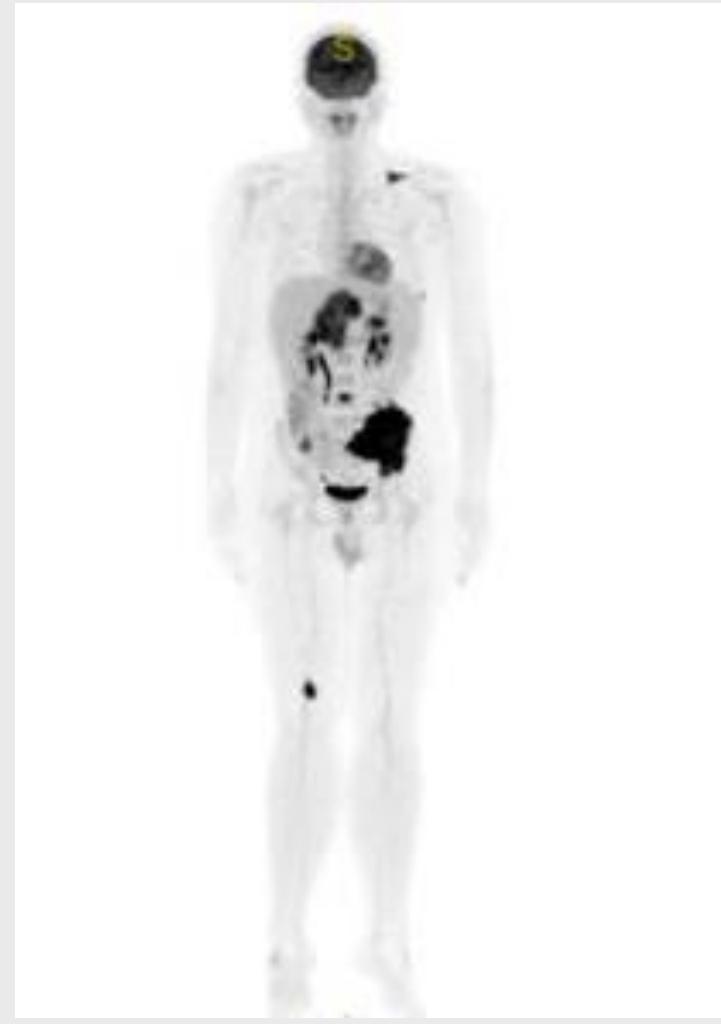
GATA3 : marquage nucléaire faible de rares cellules tumorales.

Ki67 : 60% des cellules tumorales

Vimentine: marquage d'une partie des cellules tumorales

PDL1 : marquage intense des cellules tumorales (70%, intensité 3+).

« Carcinome indifférencié compatible avec une origine bilio pancréatique ou rénale, sans exclure une autre origine »

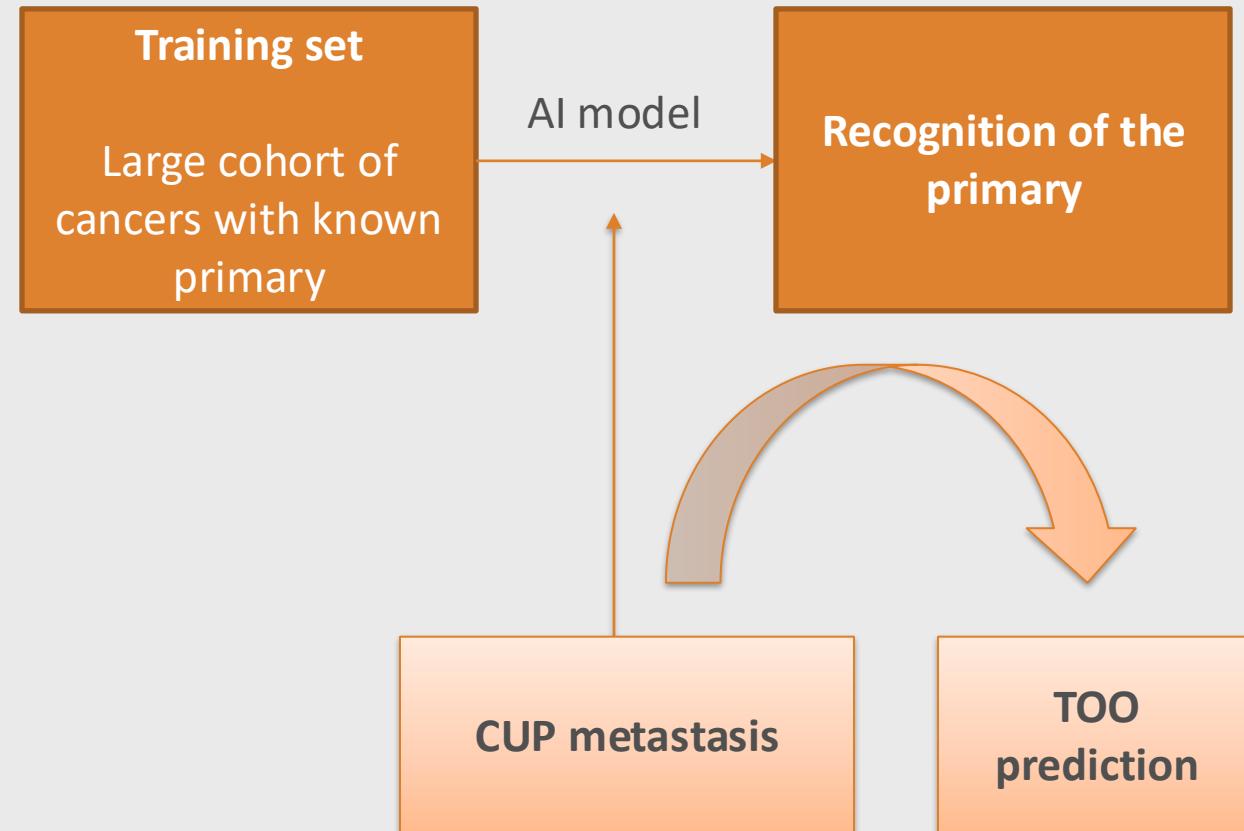


## Rationale

- Large public datasets of multiple cancer subtypes available
- Multiple types of datasets: images, molecular data

## Limits

- Datasets are mostly composed of primary tumors (and not metastases)
- Strong hypothesis: CUP metastases retain some features of their primary
- Rare cancer subtypes are missing from training datasets

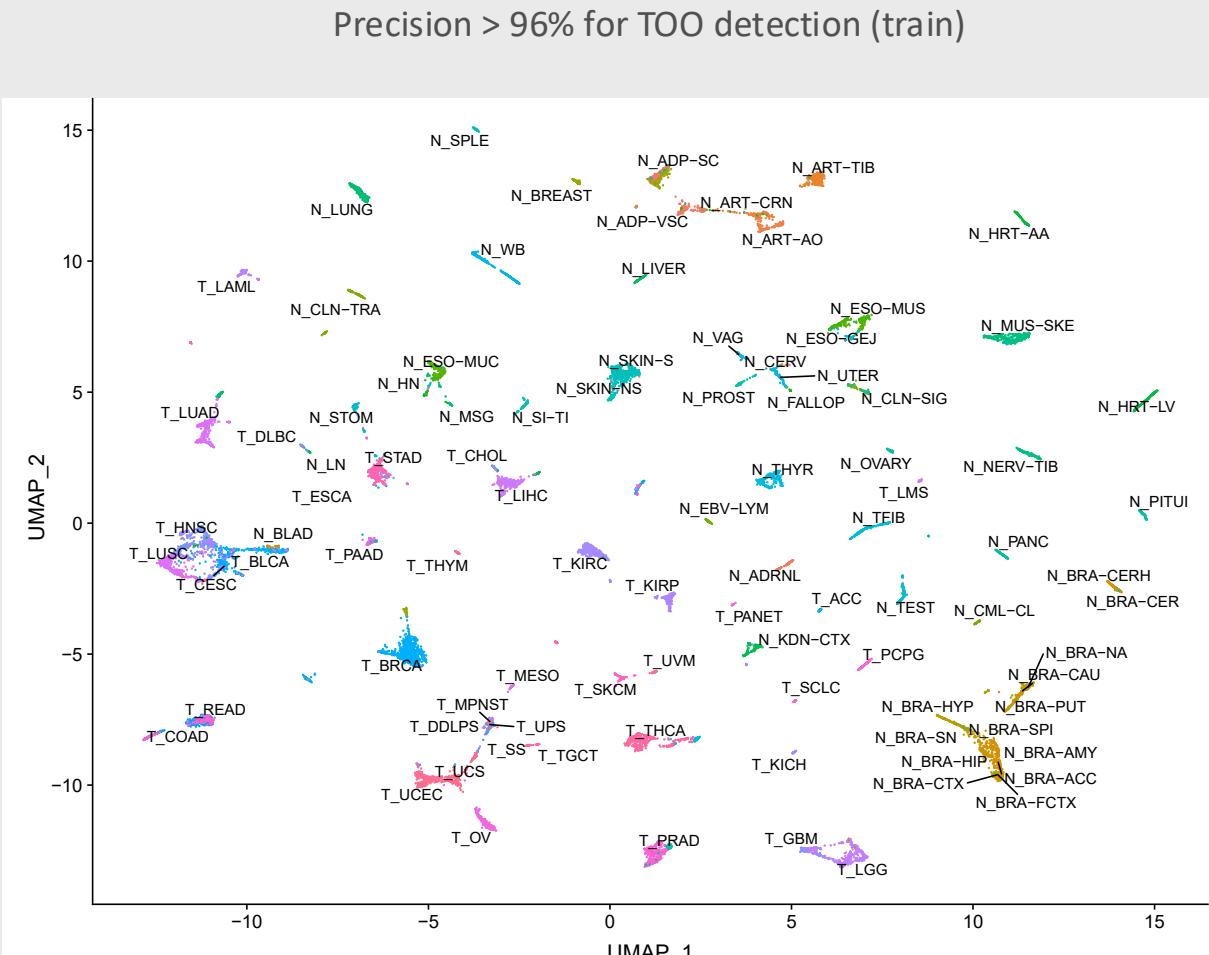
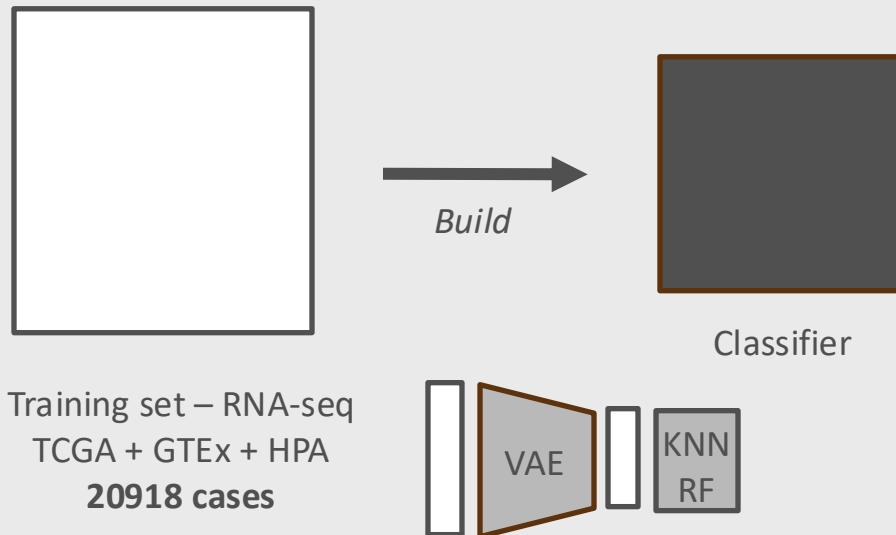


> J Mol Diagn. 2021 Oct;23(10):1380-1392. doi: 10.1016/j.jmoldx.2021.07.009. Epub 2021 Jul 26

## Identification of Tissue of Origin and Guided Therapeutic Applications in Cancers of Unknown Primary Using Deep Learning and RNA Sequencing (TransCUPomics)

Julien Vibert <sup>1</sup>, Gaëlle Pierron <sup>2</sup>, Camille Benoit <sup>3</sup>, Nadège Gruel <sup>4</sup>, Delphine Guillermot <sup>2</sup>, Anne Vincent-Salomon <sup>5</sup>, Christophe Le Tourneau <sup>6</sup>, Alain Livartowski <sup>7</sup>, Odette Mariani <sup>5</sup>, Sylvain Bauland <sup>8</sup>, François-Clément Bidard <sup>9</sup>, Olivier Delattre <sup>10</sup>, Joshua J Waterfall <sup>11</sup>, Sarah Watson <sup>12</sup>

Affiliations + expand



Vibert, J Mol Diag 2021

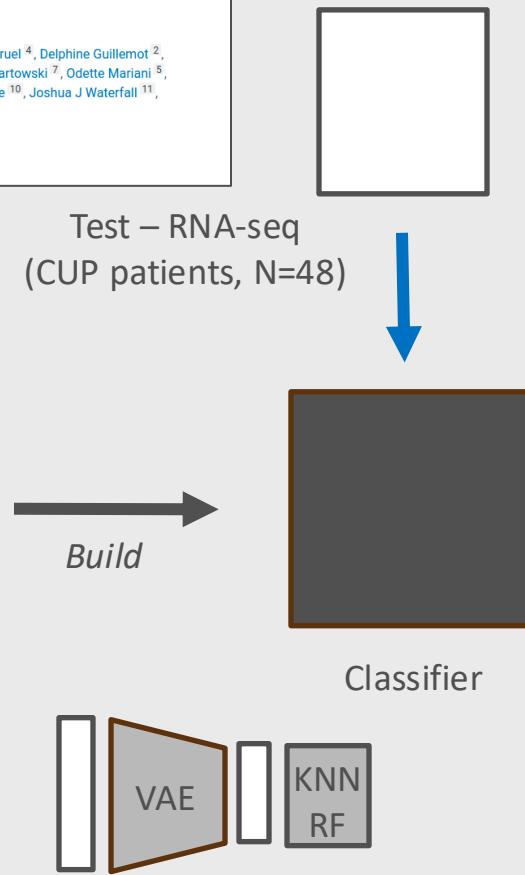
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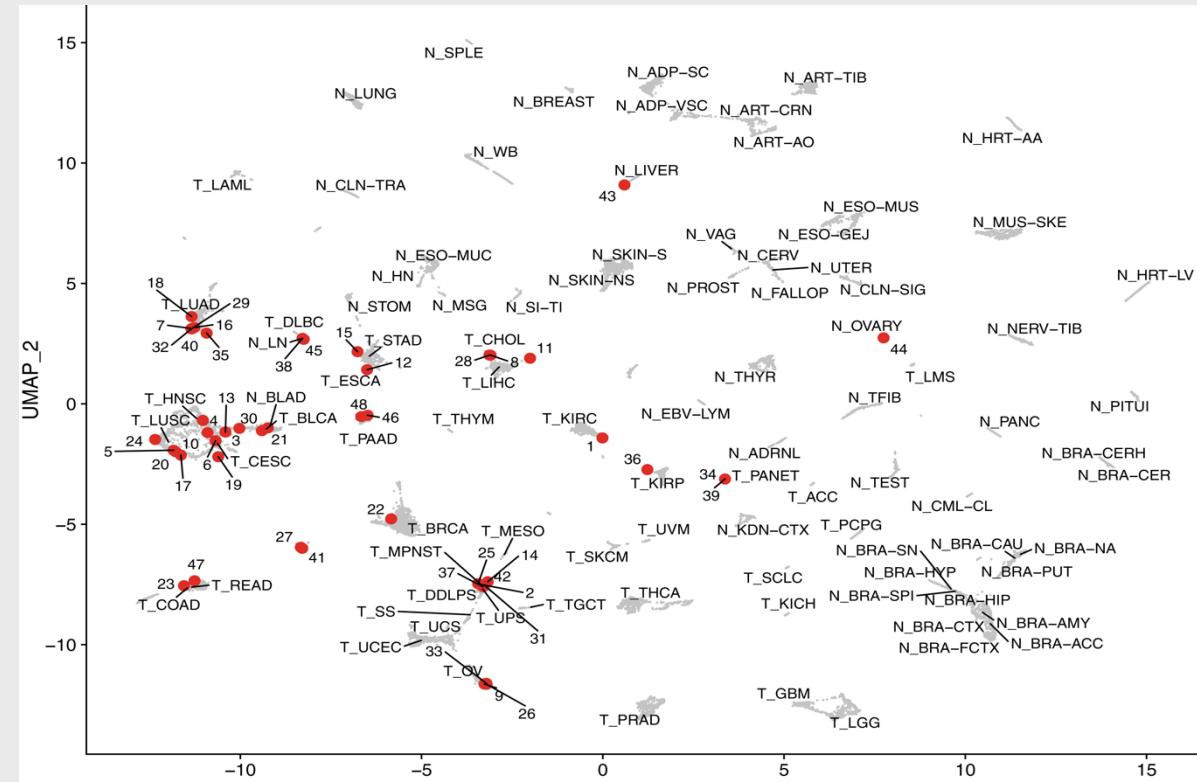
Julien Vibert <sup>1</sup>, Gaëlle Pierron <sup>2</sup>, Camille Benoist <sup>3</sup>, Nadège Gruel <sup>4</sup>, Delphine Guillemot <sup>2</sup>, Anne Vincent-Salomon <sup>5</sup>, Christophe Le Tourneau <sup>6</sup>, Alain Livartowski <sup>7</sup>, Odette Mariani <sup>5</sup>, Sylvain Baulande <sup>8</sup>, François-Clement Bidard <sup>9</sup>, Olivier Delattre <sup>10</sup>, Joshua J Waterfall <sup>11</sup>, Sarah Watson <sup>12</sup>

Affiliations + expand

PMID: 34325056 DOI: 10.1016/j.jmoldx.2021.07.009



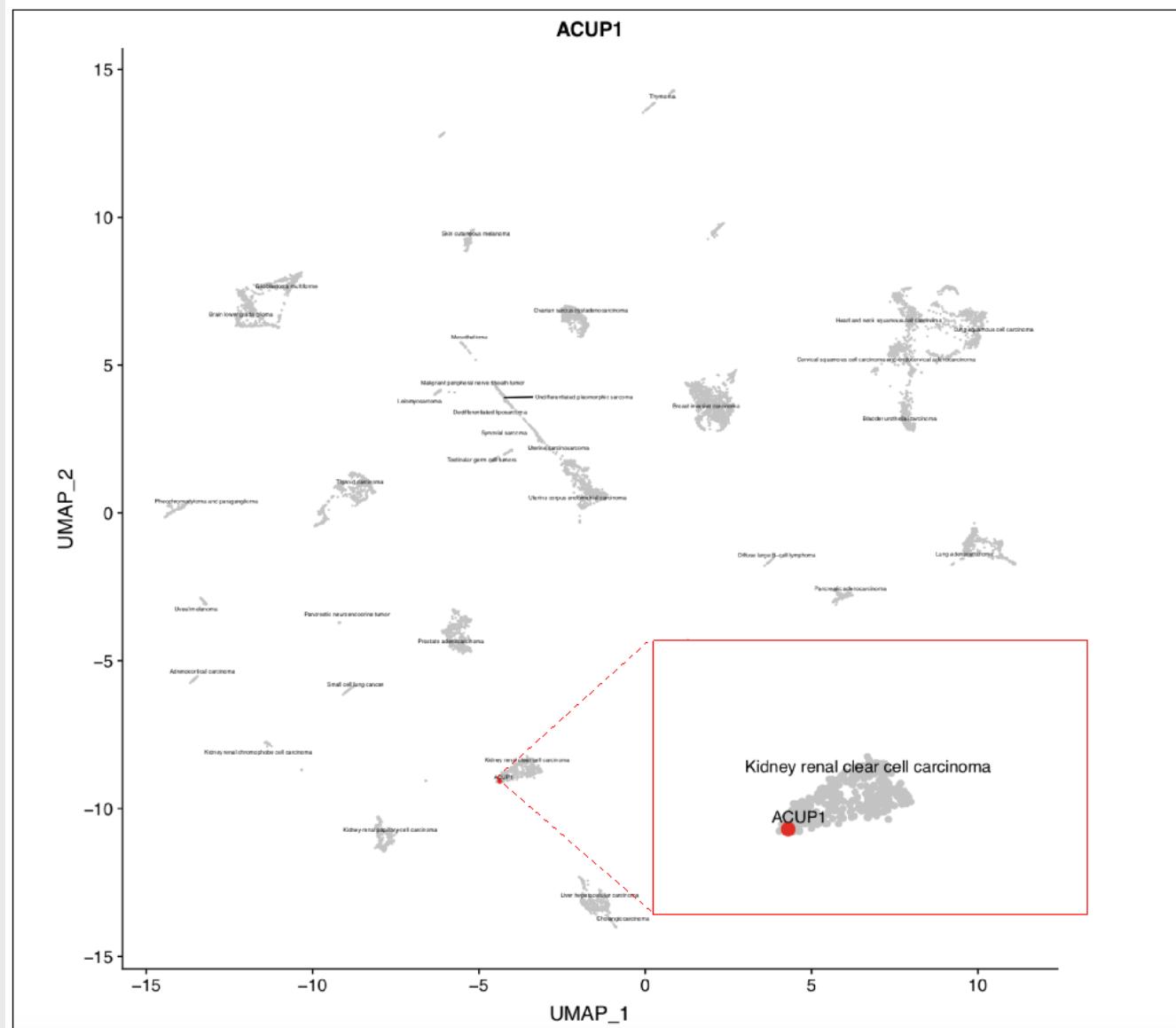
Identification of TOO (high/moderate confidence): 79%



Vibert, J Mol Diag 2021

# Faisable en routine clinique!

24

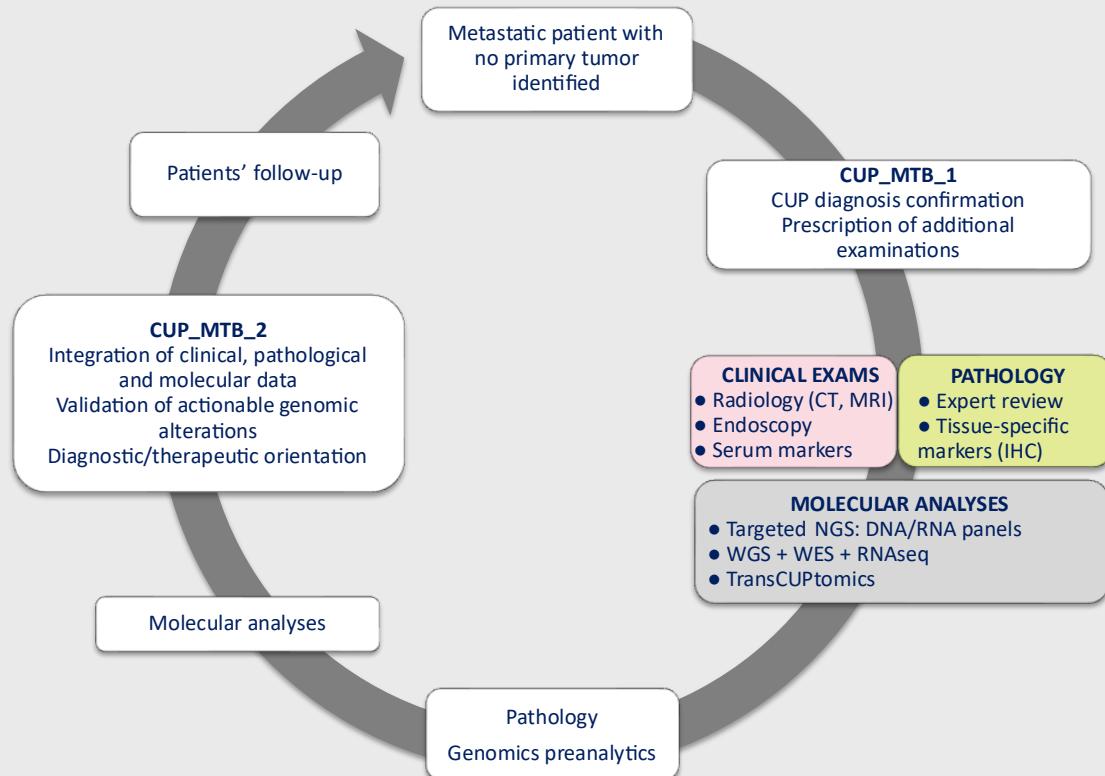


Diagnostic de carcinome rénal à cellules claires avec score > 90%

=> Orientation Immuno + anti-angiogénique

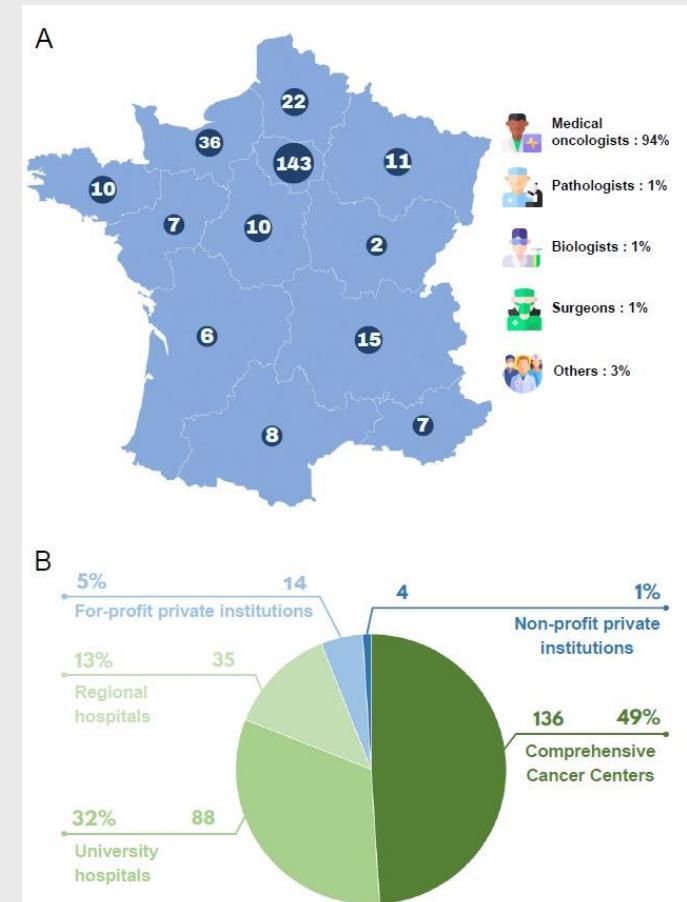
Intégration de l'outil dans le cadre de la RCP nationale CUP /PFMG 2025

## National CUP\_MTB



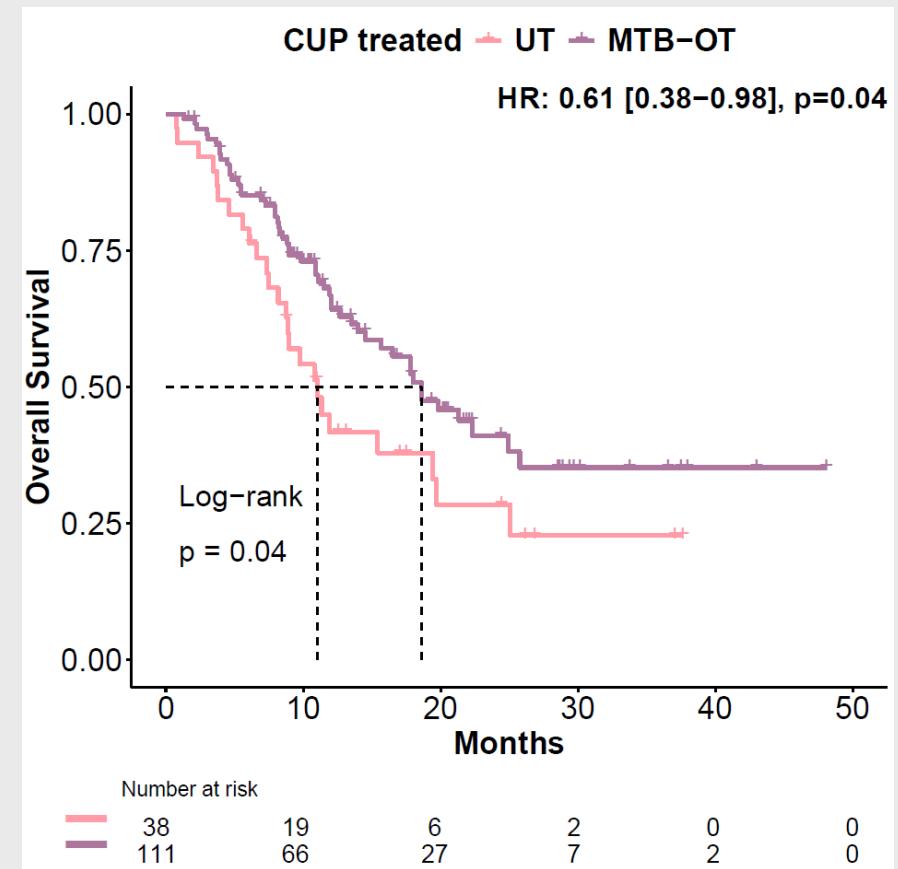
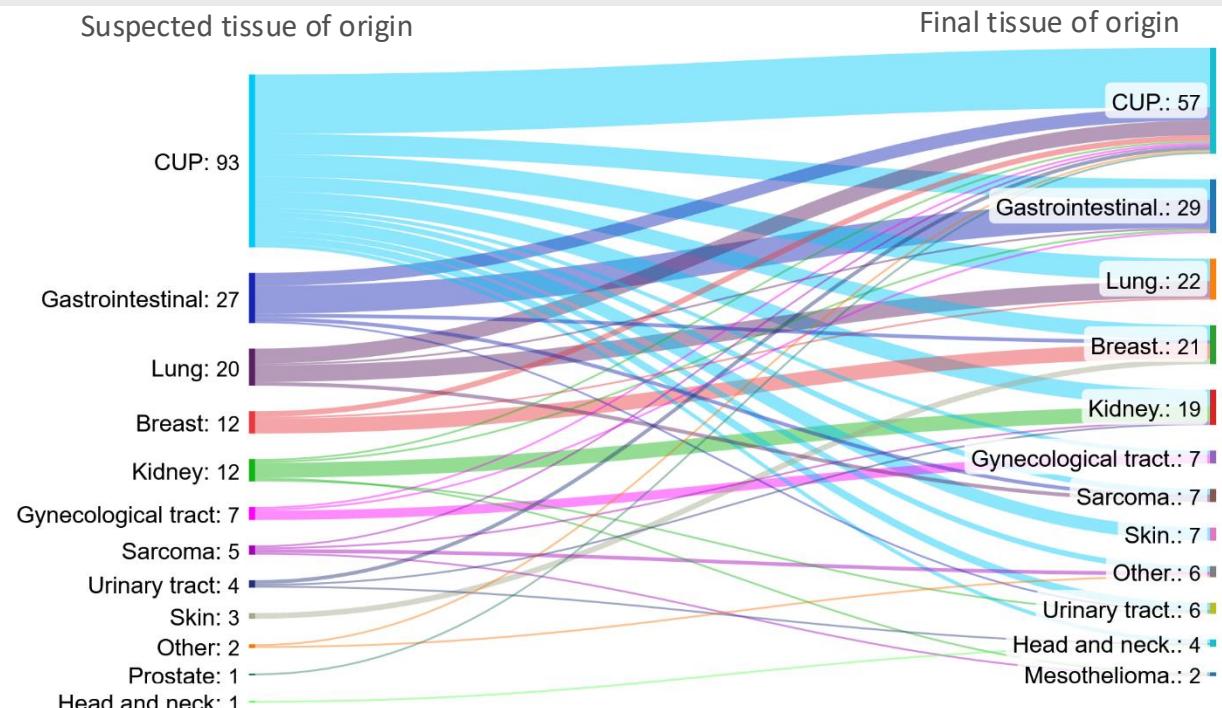
Dupain, Lancet Regional Health Europe 2025

June 2020-December 2023: N=277 pts



# Utilisation de l'IA en routine en RCP nationale CUP

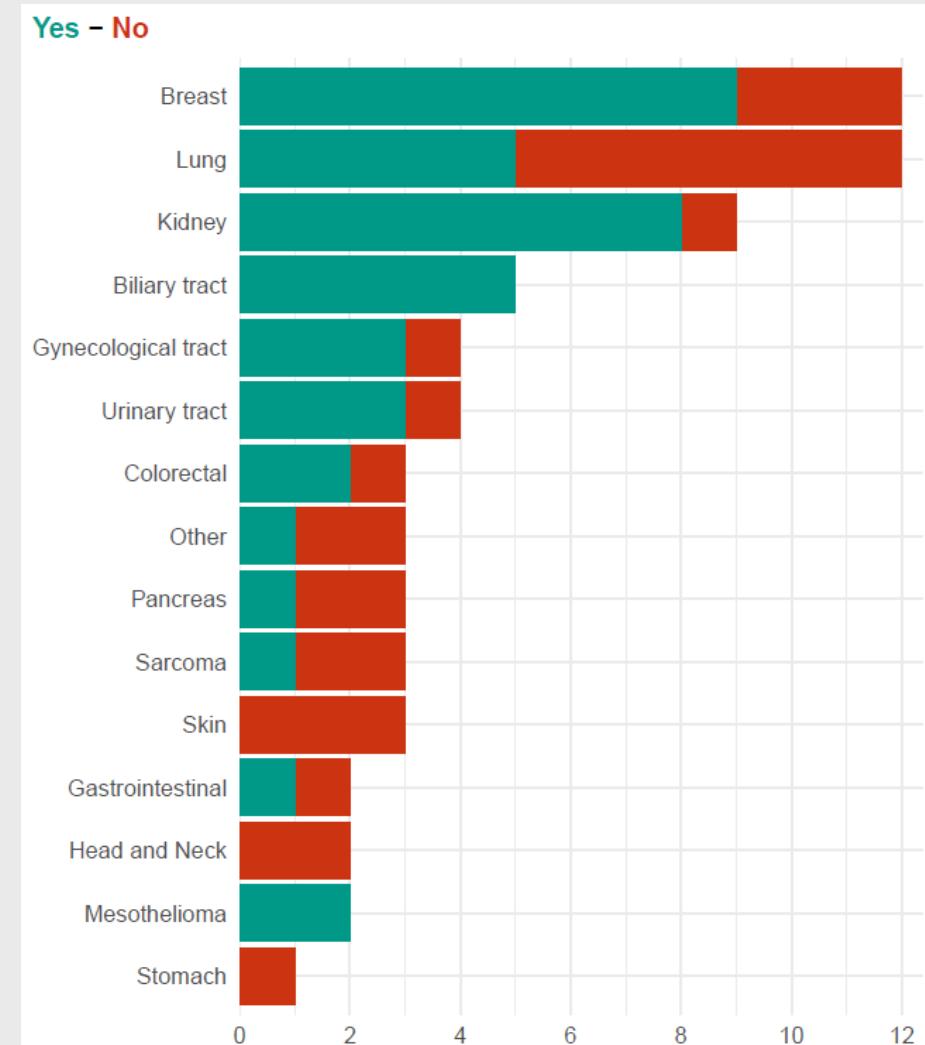
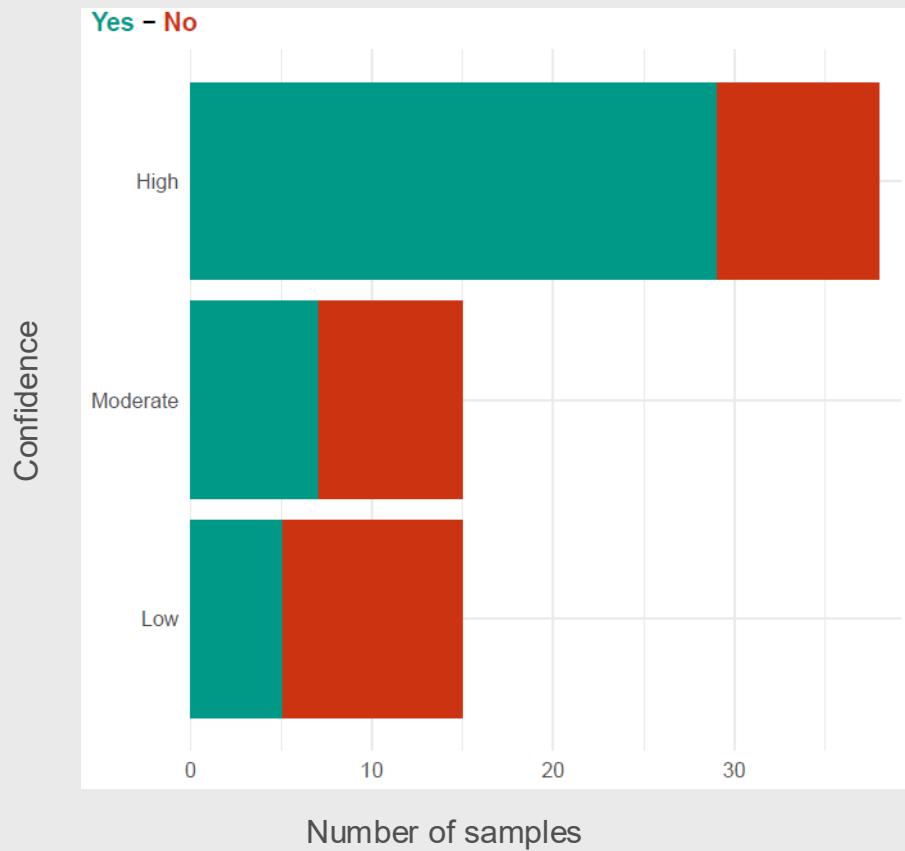
26



Dupain, Lancet Regional Health Europe 2025

# Utilité de TransCUPtomics en vraie vie

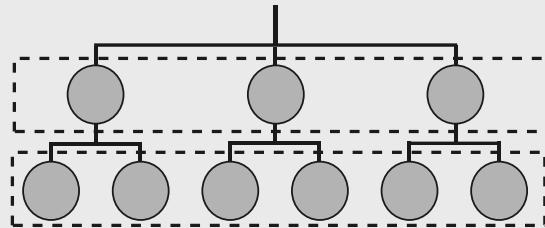
27



Dupain, *Lancet Regional Health Europe* 2025

# TransCUPtomics v2 : un modèle hiérarchique

28

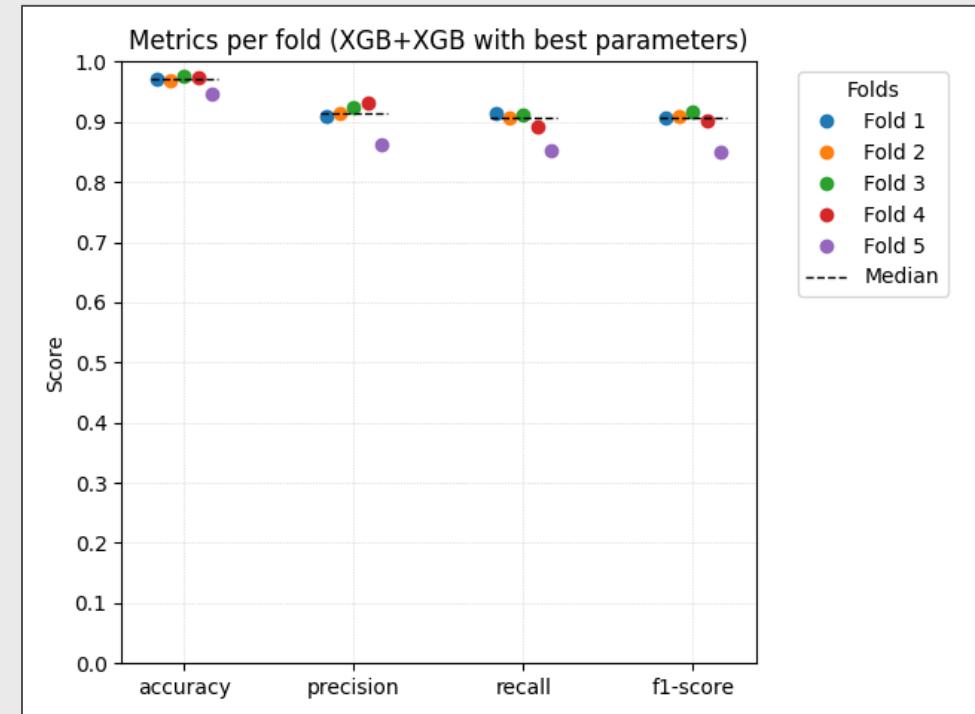
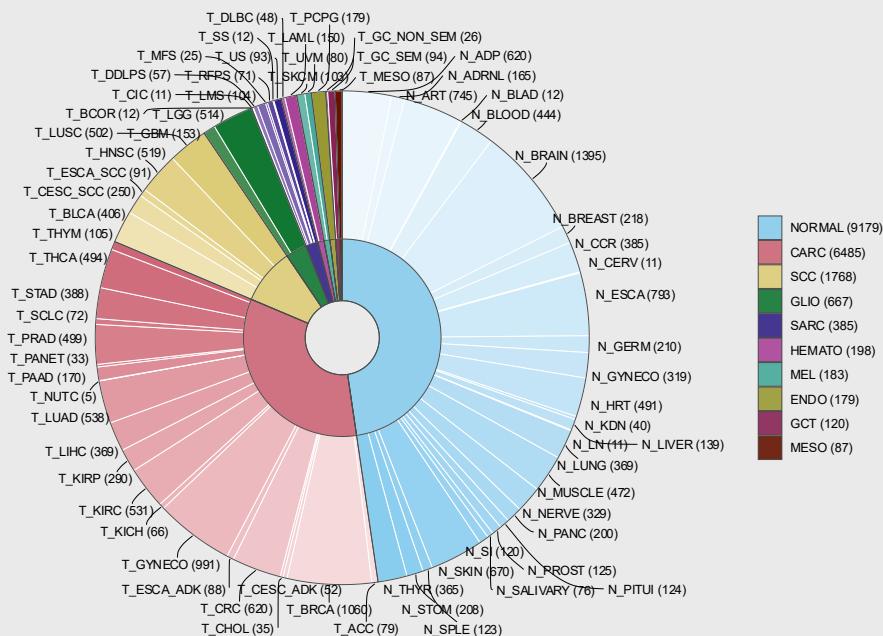


## Two-levels Hierarchy

1. Major tissue types (N=10)
2. Tissue sub-types (N=71)

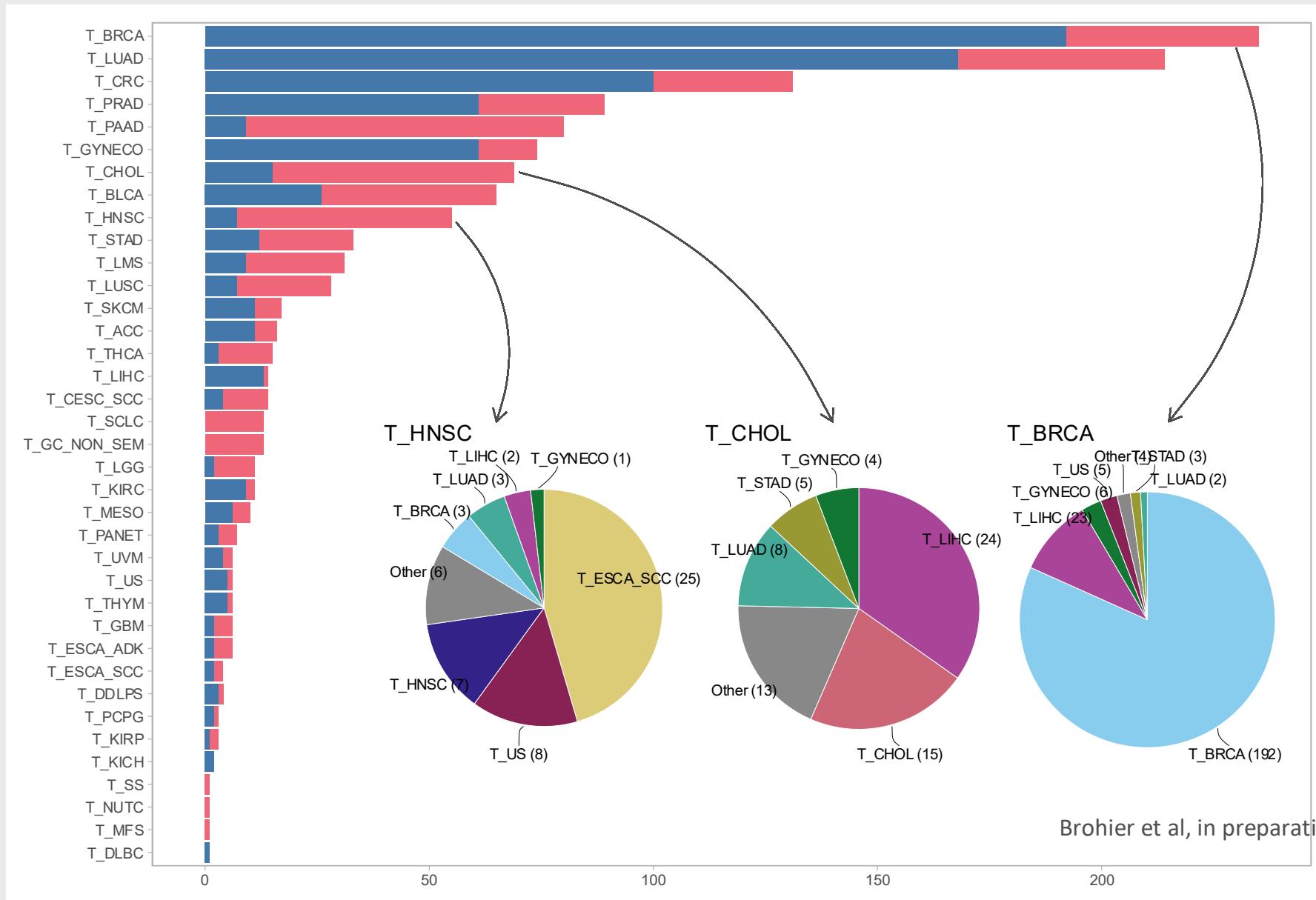
## Main interests

- Closer to clinical decision making
- Decomposition of the classification into simpler sub-tasks
- Reduces class imbalance issues



Brohier et al, in preparation (DO NOT POST)

# Validation sur des cohortes indépendantes métastatiques



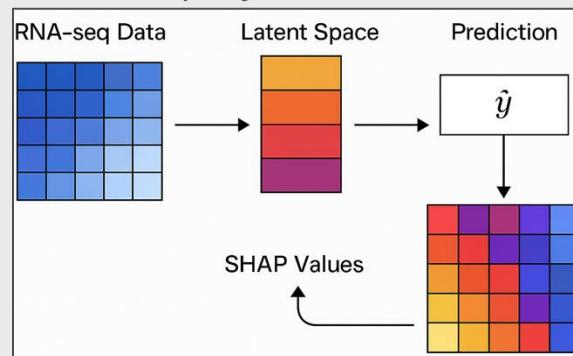
# Fournir une interprétabilité des prédictions

Latent SHAP (SHapley Additive exPlanations) aims to extract **biologically meaningful patterns** from machine learning models trained on RNA-seq data, by learning a **structured, interpretable latent space**.

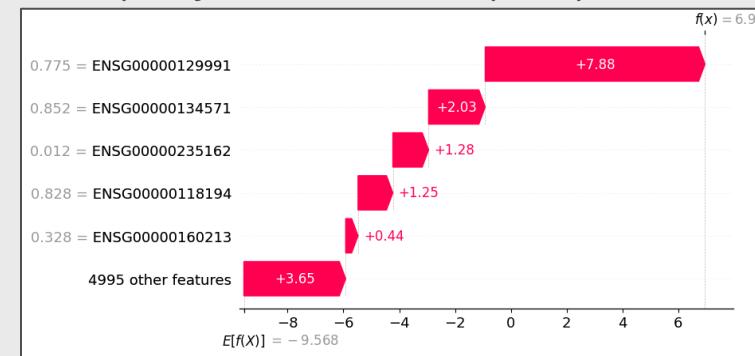
Limitations of SHAP application on RNA-seq data :

- High dimensionnality
- Strong correlation between features

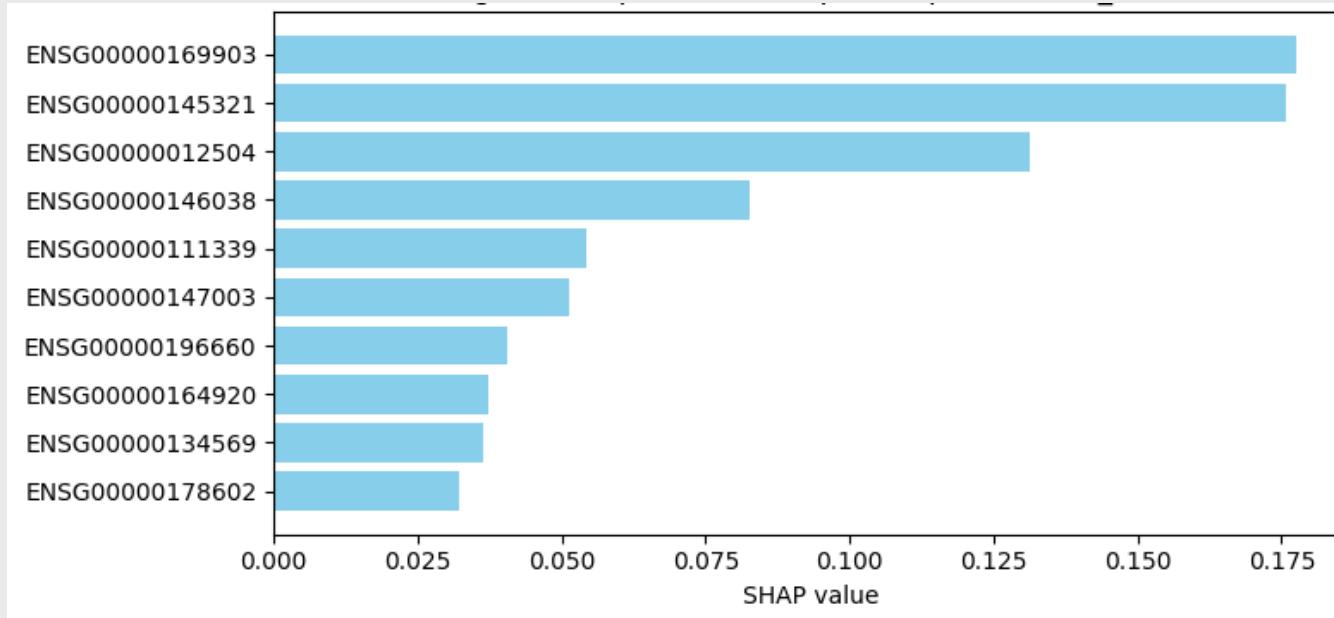
*Main concept of Latent SHAP (Bitton, Malach et al. 2022)*



*Example of SHAP values to explain predictions*



List of the 10 genes that have the heaviest weight in the prediction



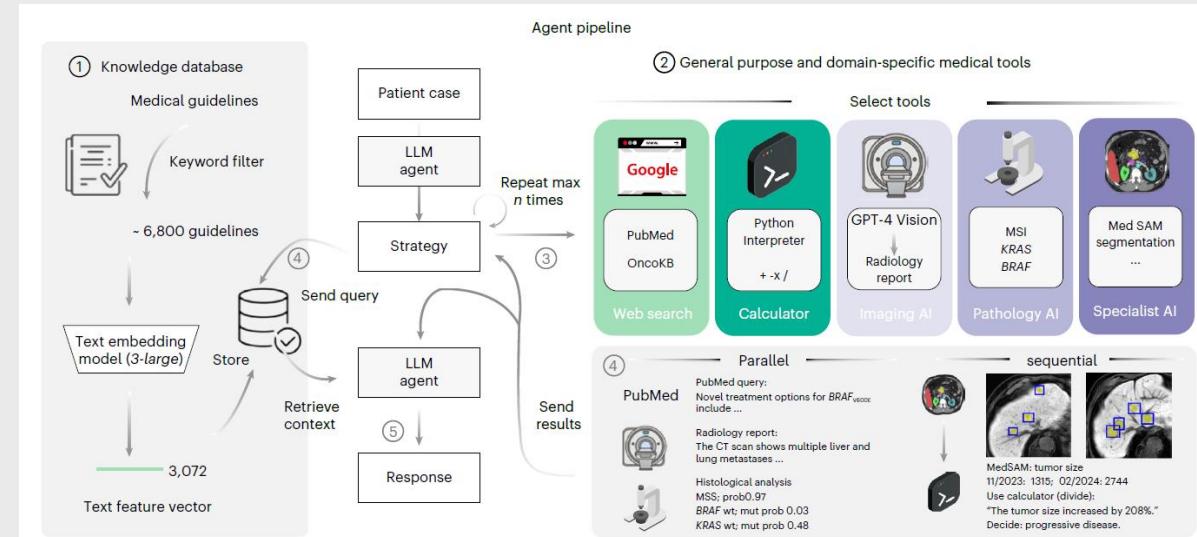
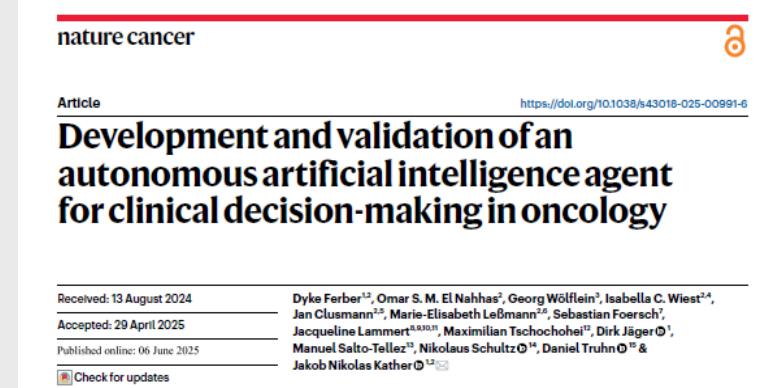
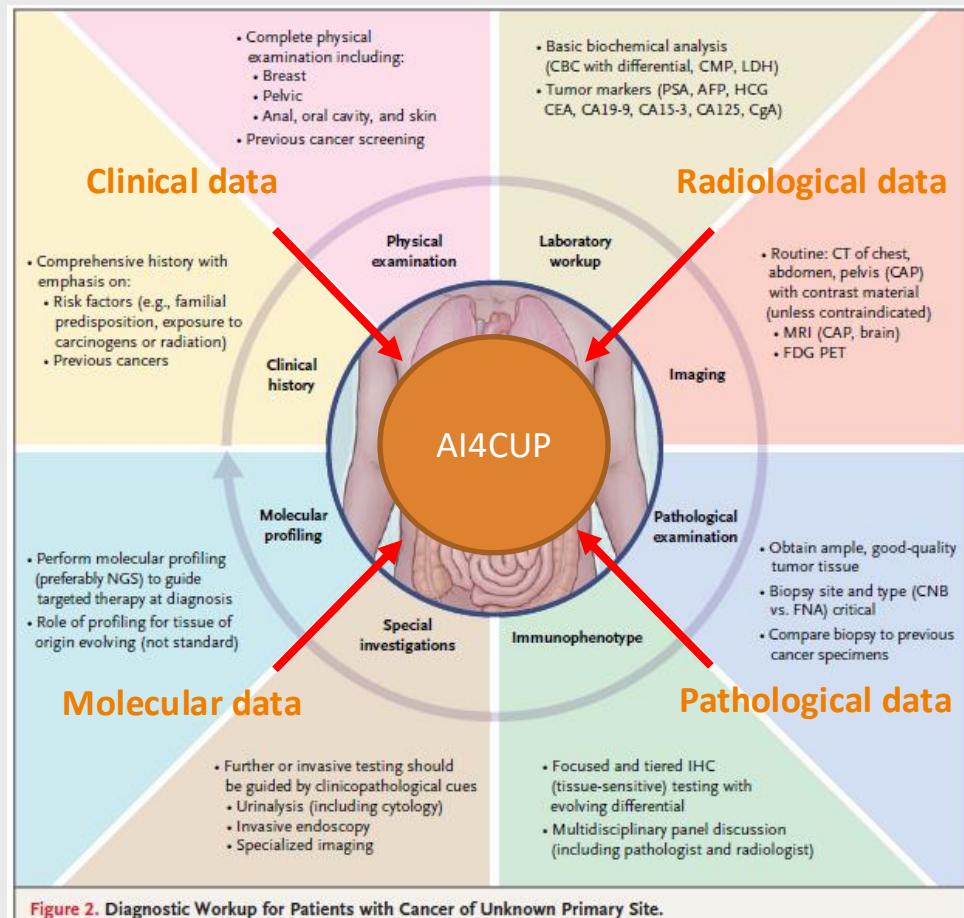
*T\_CHOL : Cholangiocarcinoma*

- **ENSG00000169903 (TM4SF4)** : proliferation and migration of epithelial cells:
- **ENSG00000012504 (NR1H4 / FXR)** : regulation of bile acids and liver metabolism

Brohier et al, in preparation (DO NOT POST)

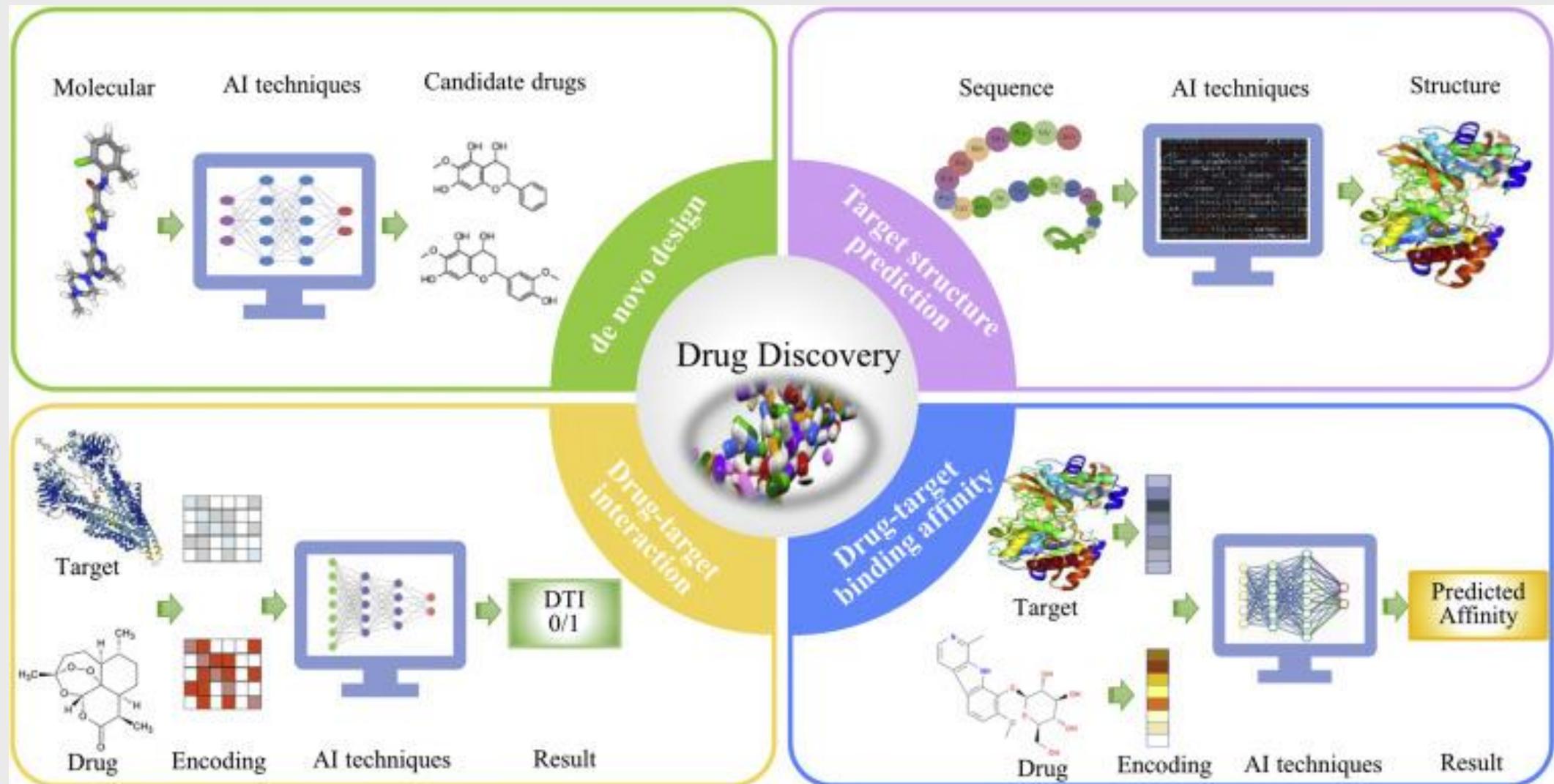
# Prochaines étapes : classification multimodale et agents IA

32



# Le futur: créer de nouvelles molécules grâce à l'IA

33



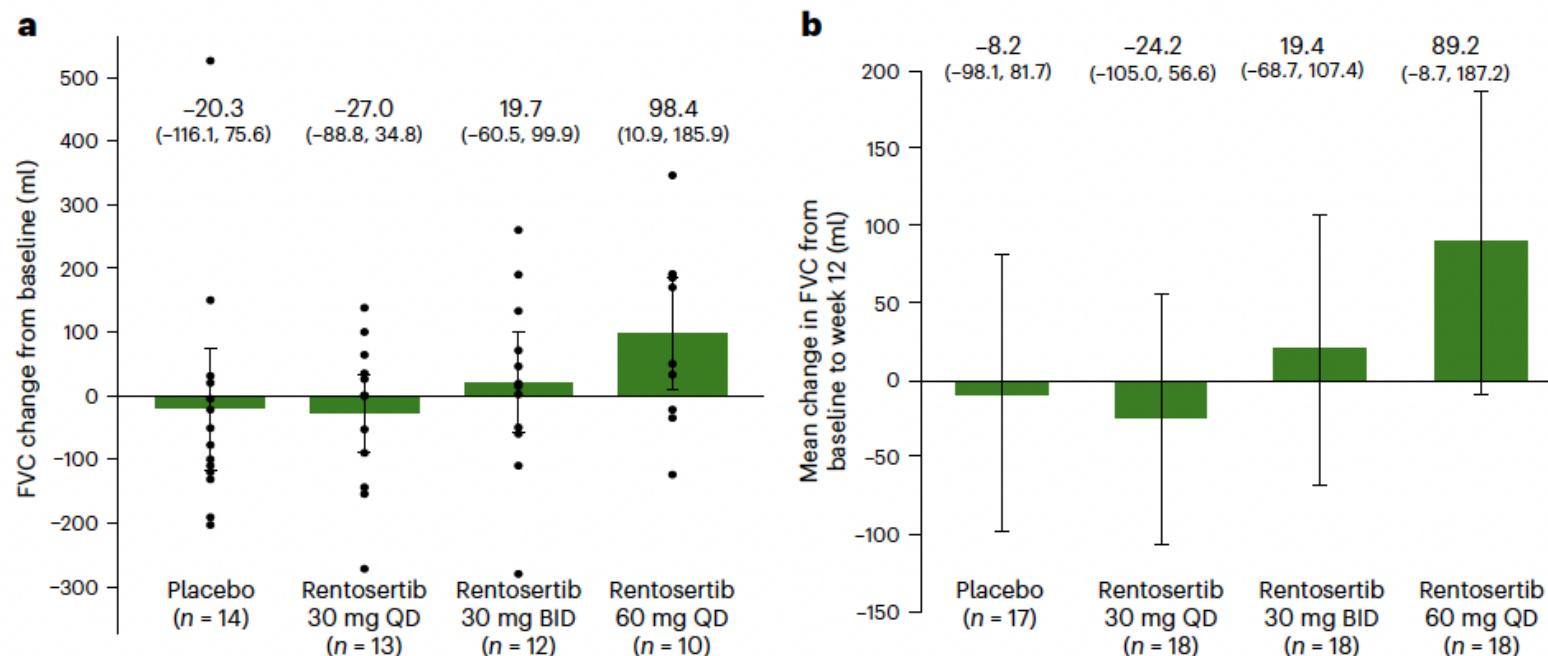
Chen, 2023

## A generative AI-discovered TNK inhibitor for idiopathic pulmonary fibrosis: a randomized phase 2a trial

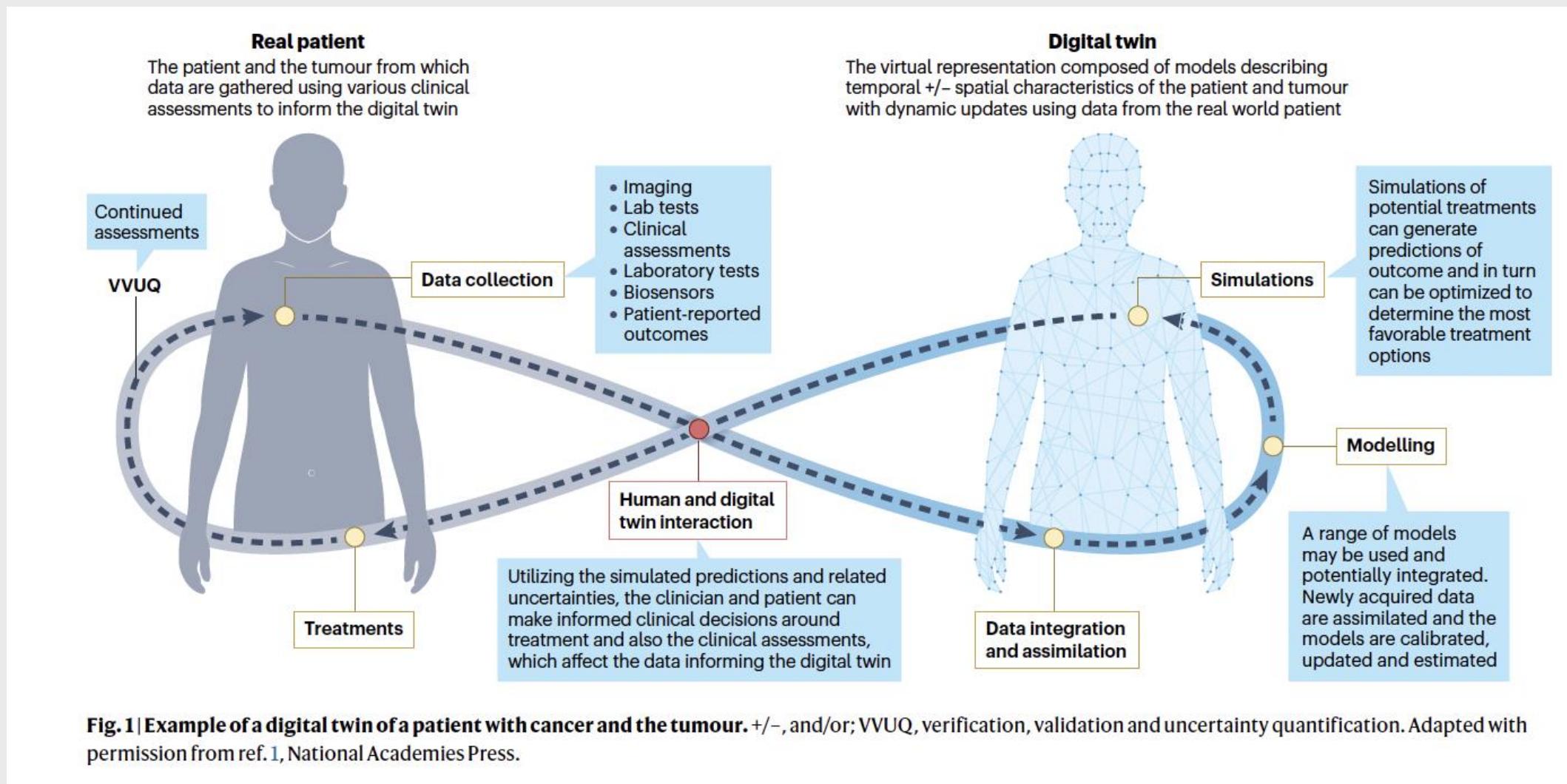
Received: 19 December 2024

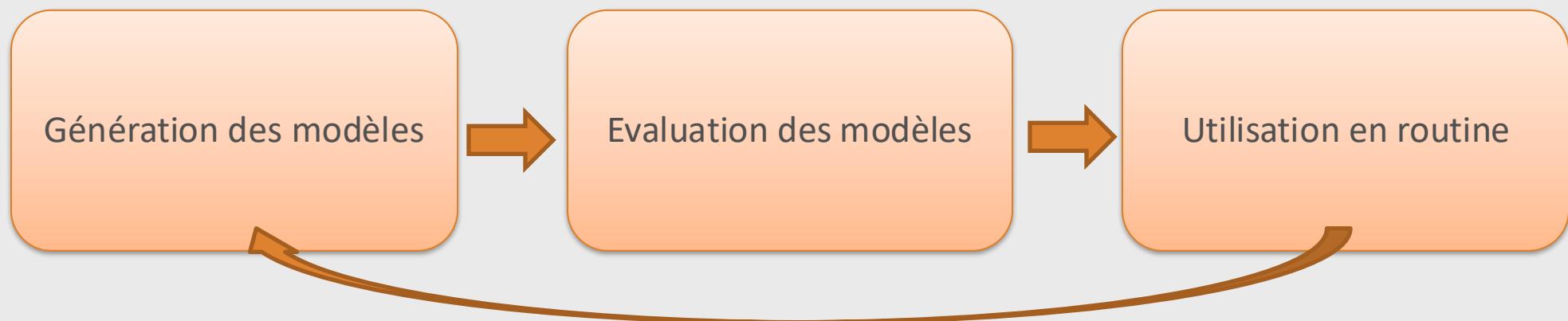
A list of authors and their affiliations appears at the end of the paper

Accepted: 25 April 2025



**Fig. 2 | Changes in FVC ± 95% CI after 12 weeks of rentosertib treatment compared to baseline.** a, The absolute change in FVC ± 95% CI. b, The absolute change in FVC ± 95% CI ANCOVA model with multiple imputation assuming missing at random (MAR).





- **Big data « utiles »**
  - qualité/homogénéité/représentabilité
- **Sources de données et aspects juridiques**
- Stockage des données

- Par qui, quand et comment?
- Robustesse/ vraie vie
- Autorité de régulation

- Formation des médecins
- Aspect user-friendly
- IA « explicable »
- Data scientists

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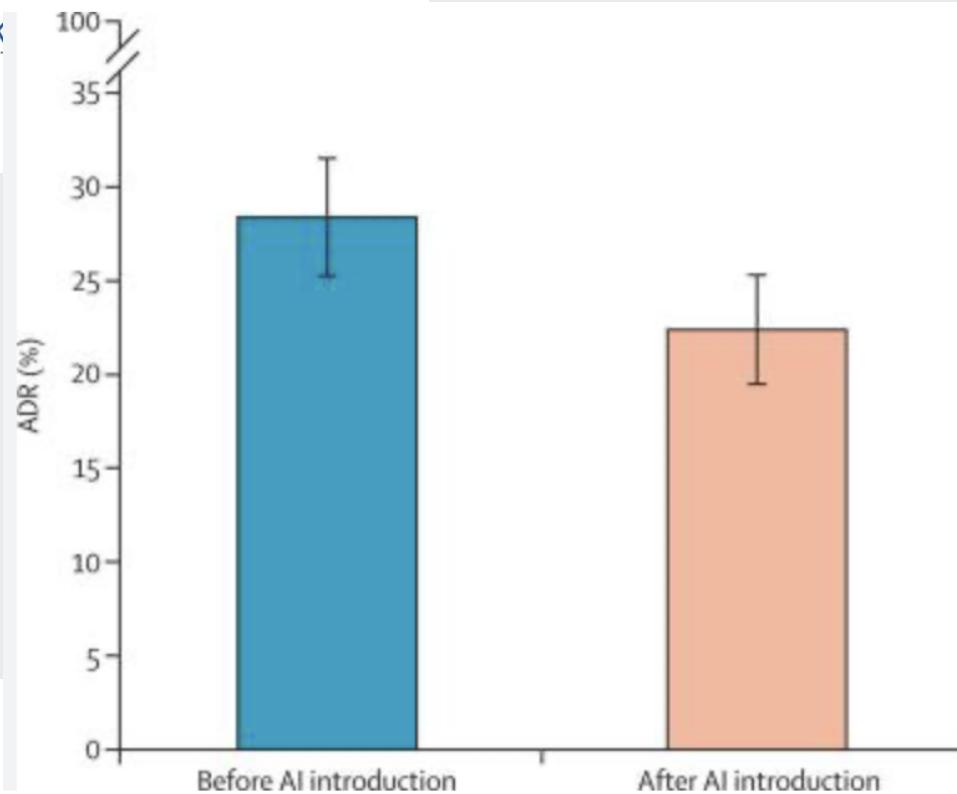
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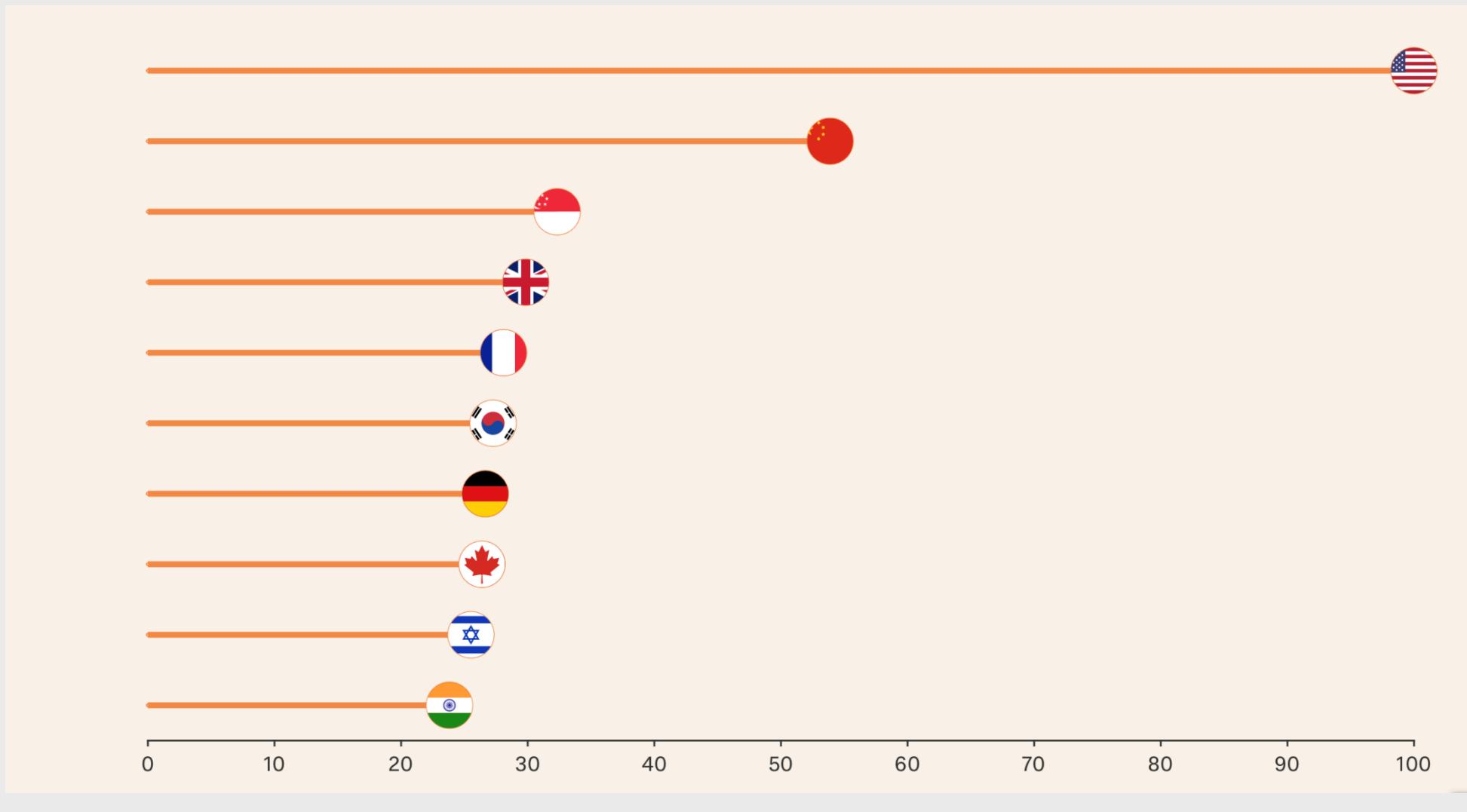
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### Endoscopist deskilling risk after exposure to artificial intelligence in colonoscopy: a multicentre, observational study

Krzysztof Budzyń, MD<sup>a,b</sup> · Marcin Romańczyk, MD<sup>a,b</sup>   · Diana Kitala, PhD<sup>c</sup> · Paweł K. Marek Bugajski, MD<sup>e</sup> · Hans O Adami, MD<sup>f,g</sup> · et al. Show more

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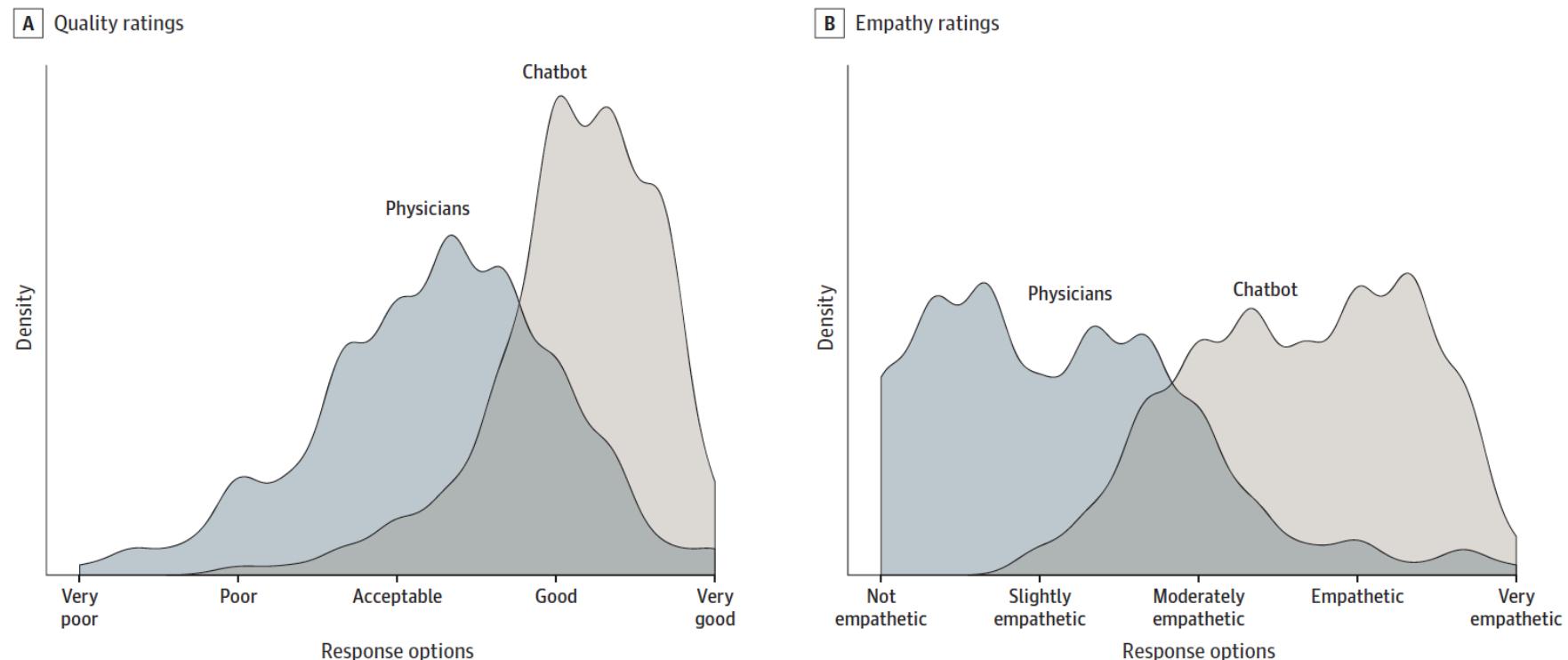




# Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum

John W. Ayers, PhD, MA; Adam Poliak, PhD; Mark Dredze, PhD; Eric C. Leas, PhD, MPH; Zechariah Zhu, BS; Jessica B. Kelley, MSN; Dennis J. Faix, MD; Aaron M. Goodman, MD; Christopher A. Longhurst, MD, MS; Michael Hogarth, MD; Davey M. Smith, MD, MAS

**Figure. Distribution of Average Quality and Empathy Ratings for Chatbot and Physician Responses to Patient Questions**



Kernel density plots are shown for the average across 3 independent licensed health care professional evaluators using principles of crowd evaluation. A, The overall quality metric is shown. B, The overall empathy metric is shown.



“Dans la vie, rien  
n'est à craindre, tout  
est à comprendre.”

Marie Curie, physicienne  
(1867-1934)

# Collaborations et soutiens

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