CLUB VITA and Nationwide

THE RISK OF **LIVING LONGER**

Thank you for joining us – the webinar will start shortly

Douglas and Uli ask the ultimate question of human longevity for financial institutions:

How long can we go?

Series program

Session 1 April 16th, 2024	*An introduction to the question of human longevity: how long can we go?*	• Dan Ryan, Just Group • Phil Newman, Longevity.technology	Recording here
Session 2 May 7th, 2024	*The biology of aging*	• Richard Faragher, University of Brighton • Niharika Duggal, University of Birmingham	Recording here
Session 3 May 28th, 2024	*Cancer research*	• Gao Xiao, SCOR • Catherine Pickworth, Cancer Research UK	Recording here
Session 4 June 18th, 2024	*Biological clocks*	• Peter Joshi, Humanity Inc • John Schoonbee, Swiss Re	Recording here
Session 5 July 9th, 2024	**Using Big Data and AI to improve and advance longevity**	• Gregg TeHennepe, The Jackson Laboratory • Steven Baxter, Club Vita	Today!

For full details and registration for the series,
visit: www.clubvita.net/uk/events or follow http://linkedin.com/company/club-vita

THE RISK OF **LIVING LONGER**

Session 5: Using Big Data and AI to improve and advance longevity

Douglas Anderson
(Chair)

Founder & Chief Visionary Officer

Club Vita

Ulrich Stengele
(Chair)

Chief Actuary

Nationwide Financial

Gregg TeHennepe
(Panelist)

Senior Director, Computational Sciences

The Jackson Laboratory

Steven Baxter
(Panelist)

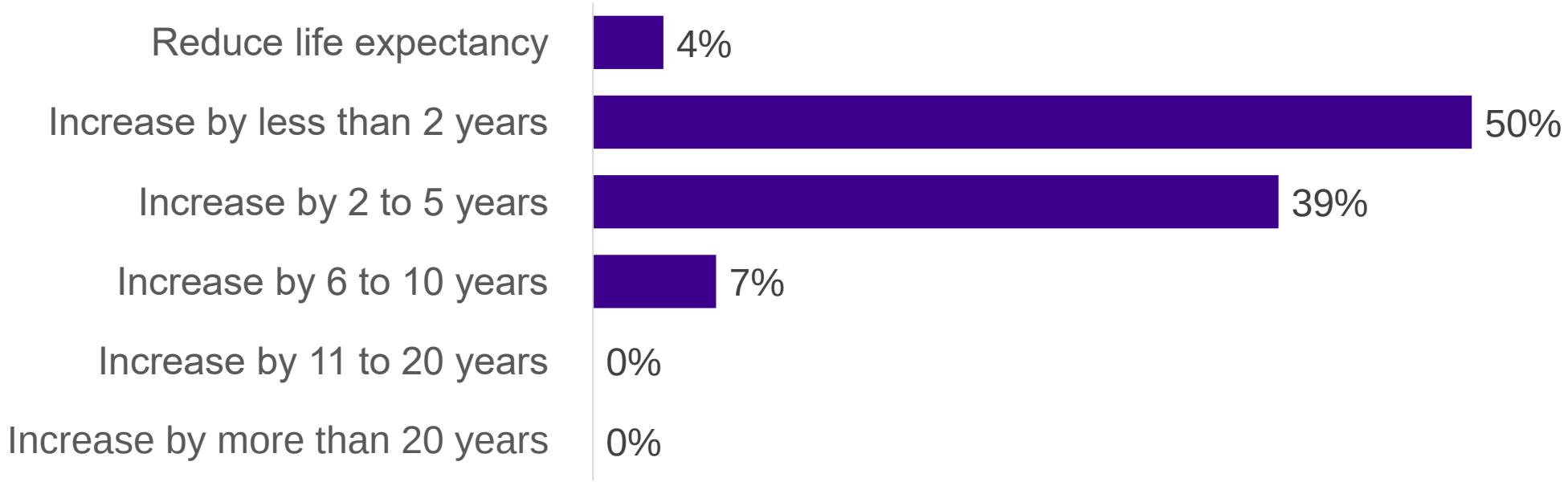
Head of Innovation and Development

Club Vita

CLUB VITA

Poll question

"How will big data and AI contribute to changes in life expectancy for a 60-year-old in 20 years' time?"



CLUB VITA

Big Data & AI

Medical records

Images

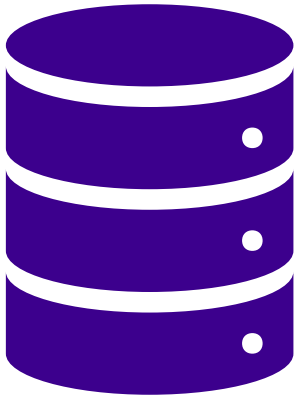
Genome sequencing

Physical activity

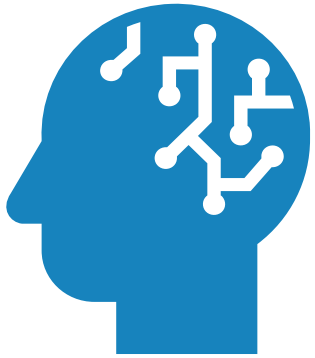
Diet

…

Big Data



Artificial Intelligence



Algorithms

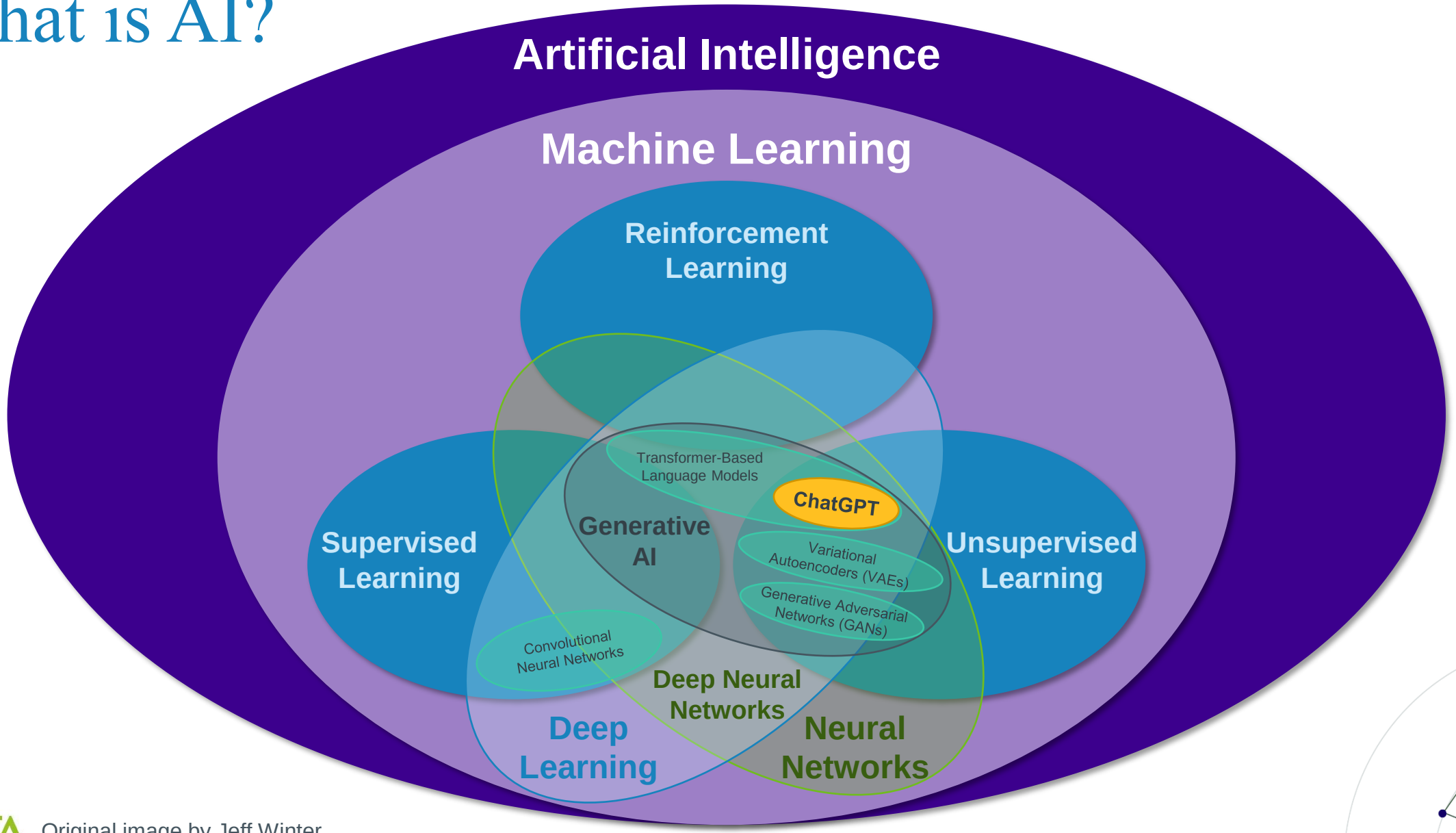
Pattern recognition

Image cleaning

Language processing

…

What is AI?

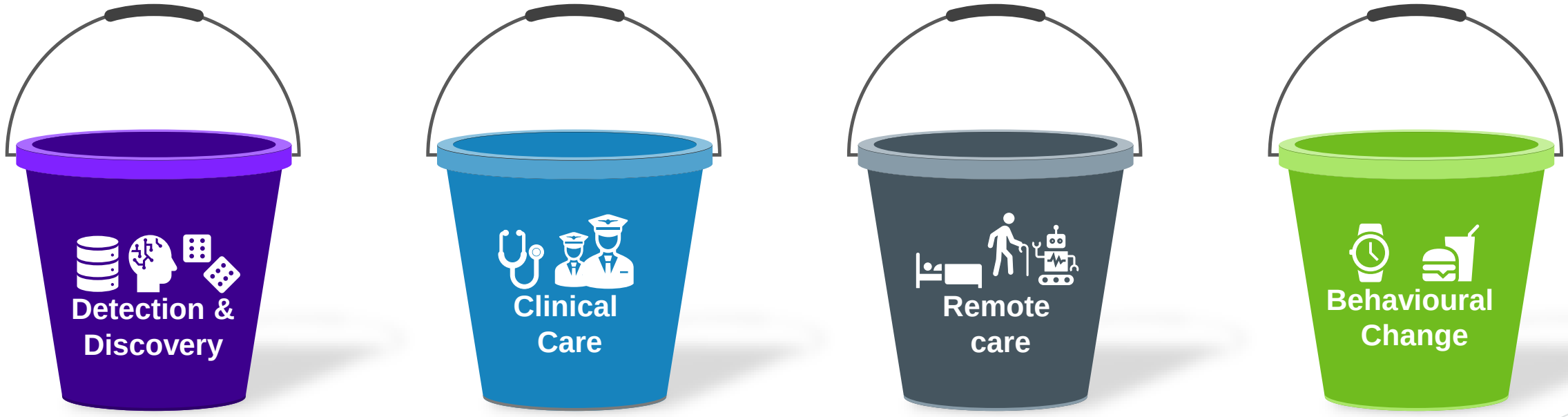


Original image by Jeff Winter

Types of machine learning

- Image redacted for copyright.
- Image available on Artificial Intelligence in Cardiac Imaging - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Types-of-Machine-Learning-with-Examples-of-Respective-Use_fig1_339462675 . Accessed July 9.

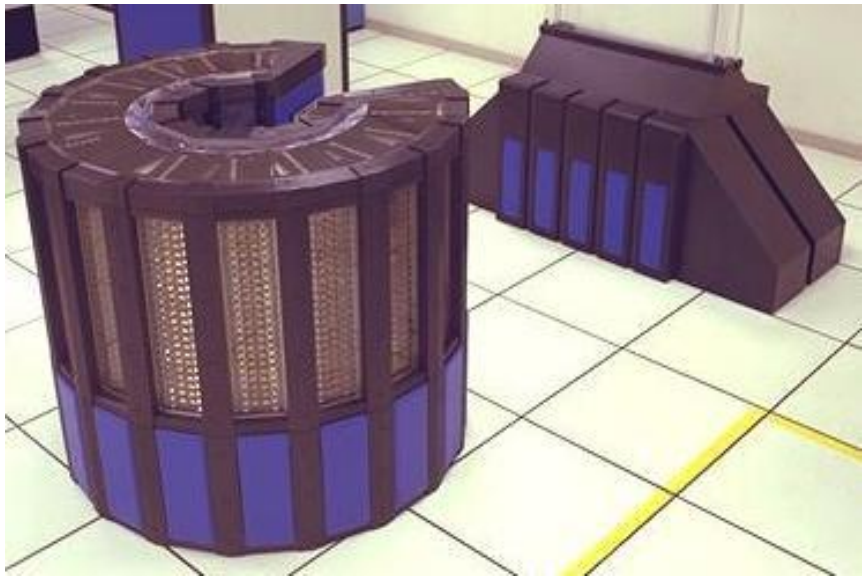
How might “AI” impact healthcare & longevity?



About JAX

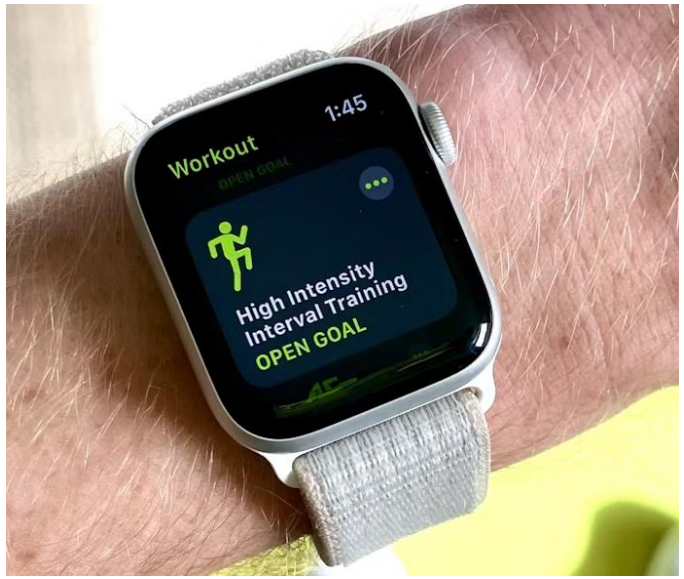
We’re an independent, biomedical research institution that empowers the global biomedical community with research tools, data resources & education.

Cray 2 Supercomputer (~1985)



Source: NASA

X 2 =



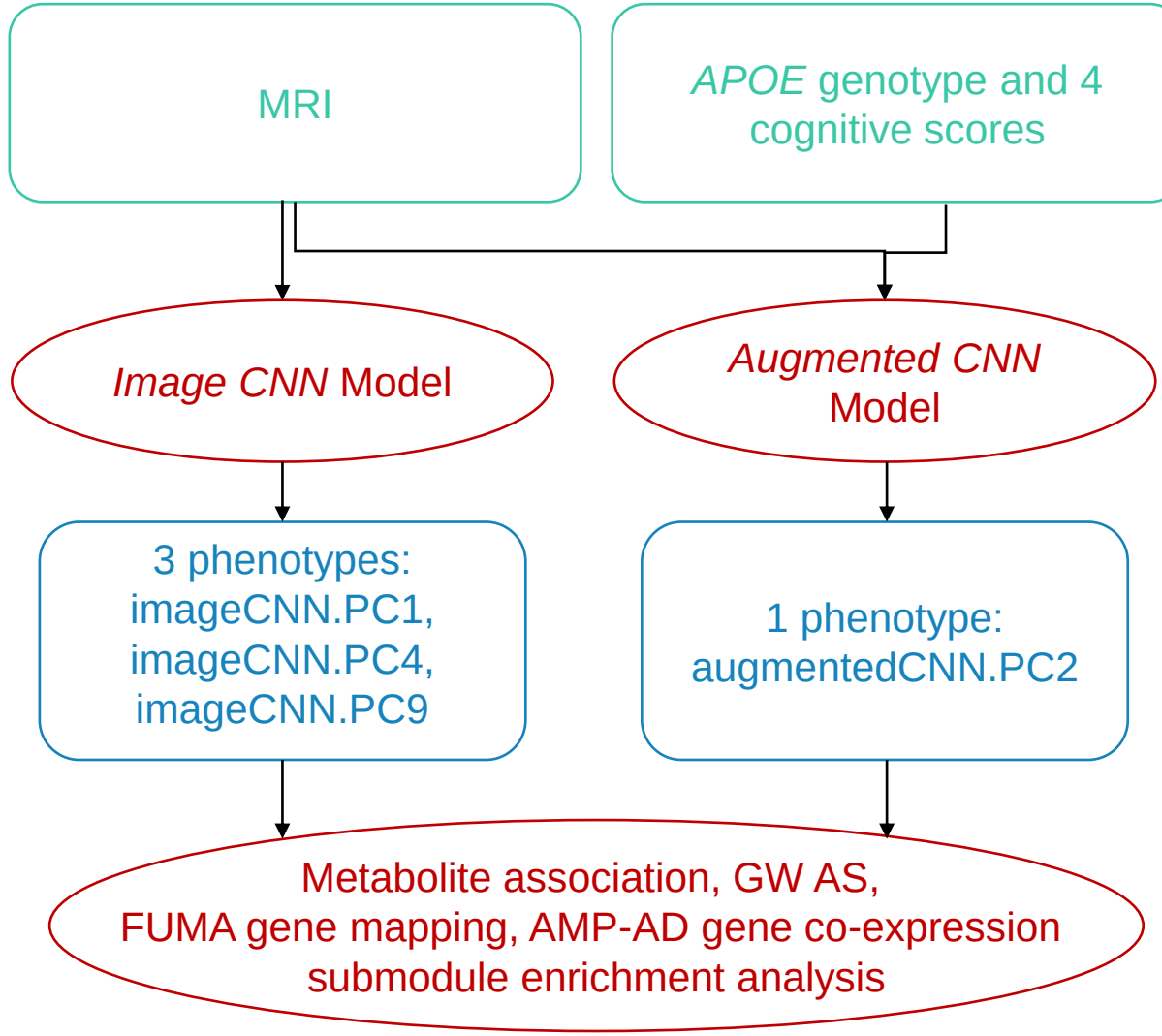
Source: Unsplash

Cost of Sequencing a Human Genome

- Image redacted for copyright.
- Image available on Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Genome Sequencing Program (GSP) Available at: **www.genome.gov/sequencingcostsdata**. Accessed July 9.

For help understanding the logarithmic scale see here: Exponential growth and an appreciation for the logarithm

Transfer learning-trained convolutional neural networks identify novel MRI biomarkers of Alzheimer's disease progression.



Legend:

input | *analysis* | derived phenotypes

Li Y, Haber A, Preuss C, John C, Uyar A, Yang HS, Logsdon BA, Philip V, Karuturi RKM, Carter GW; Alzheimer's Disease Neuroimaging Initiative. Transfer learning-trained convolutional neural networks identify novel MRI biomarkers of Alzheimer's disease progression. Alzheimers Dement (Amst). 2021 May 14;13(1):e12140. doi: 10.1002/dad2.12140. PMID: 34027015; PMCID: PMC8120261.

Harnessing large language models (LLMs) for candidate gene prioritization and selection

Detection & Discovery

- Image redacted for copyright.
- Image available here: https://doi.org/10.1186/s12967-023-04576-8

Toufiq, M., Rinchai, D., Bettacchioli, E. *et al.* Harnessing large language models (LLMs) for candidate gene prioritization and selection. *J Transl Med* **21**, 728 (2023). https://doi.org/10.1186/s12967-023-04576-8

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“AMR is one of the top 10 global public health threats facing humanity” WHO

10^8

10^{60}

Detection & Discovery

Source of WHO quote: https://www.who.int/docs/default-source/antimicrobial-resistance/amr-factsheet.pdf
Additional information and source of figures: Stanford Medicine News Center

CLUB VITA

"…we didn't build algorithms specifically for COVID; we just put them through the same pipeline of activity that we've been doing. We just turned it as fast as we could. When we think about everything we do at Moderna, we think about this platform capability. We were never going to make *one* drug; that was never the plan. The plan was always to make a whole platform around mRNA because, since it's an information-based product, all you do is change the information encoded in the molecule, and you have a completely different drug."

Dave Johnson, Moderna

Source: Me, Myself and AI: AI and the COVID-19 vaccine. An interview podcast with Dave Johnson chief data and artificial intelligence officer at Moderna. Transcript and podcast available from MIT Sloan Management review at https://sloanreview.mit.edu/audio/ai-and-the-covid-19-vaccine-modernas-dave-johnson/

Source of image: Unsplash

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AI use cases and applications

Clinical Care

New Scientist

Technology

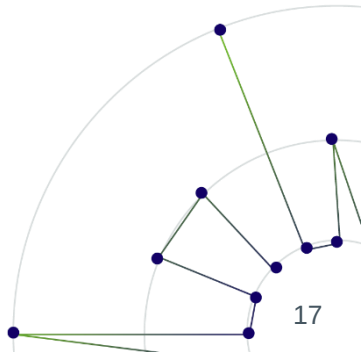
AI that determines risk of death helps save lives in

An AI trained on the heart's electrical activity alerted physicians about patients at high risk of dying, significantly reducing deaths in a clinical trial with almost 16,000 patients at two hospitals

By Jeremy Hsu

29 April 2024

Source: New Scientist



HEALTH

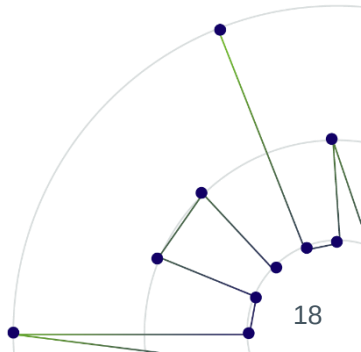
Clinical Care

ChatGPT correctly diagnosed a 4-year-old’s mysterious disease after 17 doctors failed

By Kate Hull

September 12, 2023

Source: Business Insider



- Image redacted for copyright.
- Image available here: https://www.technologyreview.com/2020/11/30/1012712/deepmind-protein-folding-ai-solved-biology-science-drugs-disease/

Source: MIT technology review

Japanese robot can lift patients from beds into wheelchairs or help them to stand up, promising “powerful yet gentle care” for the elderly

- Image redacted for copyright.

Source: Robear: the bear-shaped nursing robot who'll look after you when you get old | Robots | The Guardian

- Image redacted for copyright.

Source: https://www.genieconnect.co.uk/

The smart floor monitoring system based on the deep learning-enabled smart mats (DLES-mats)

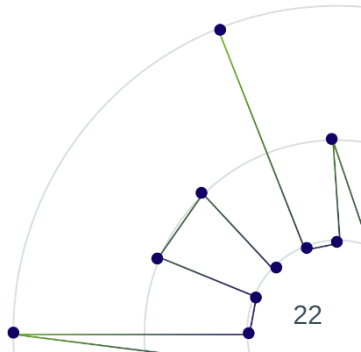
- Image redacted for copyright.

Source: Part of Fig1 extracted from Deep learning enabled smart mats as a scalable floor monitoring system

Behavioural Change

> **AI is the cornerstone of preventive medicine and health behaviour change. Everyone has unique behaviours, needs and preferences; there's no way traditional healthcare can cope with this form of complexity in providing personalised and precision care.**
>
> **– Dr Jocelyn Chew**

Source: https://www.nuhsplus.edu.sg/article/leveraging-ai-for-health-behaviour-change



Development and Application of Machine Learning-Based Digital Biomarkers for Monitoring Spontaneous Seizures in Preclinical Epilepsy Models

DIGITAL IN VIVO ALLIANCE

Jennifer Leedy[1], Nicole E. Peltier[2], Lizet Reyes Rodas[1], Manuel Lopez[1], Manuel E. Ruidíaz[2], Michael Saul[3], Natalie Bratcher-Petersen[2], Timothy L. Robertson[2,3], Brian Berridge[4]

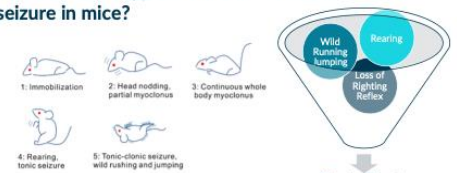
Abstract

For this work, we ran a **natural history study utilizing home-cage video data from two mouse models of Dravet Syndrome**, a severe epileptic encephalopathy. Dravet mice and wildtype littermates were weaned into video-integrated cages, where monitoring occurred from postnatal day 21 to postnatal day 50. **To identify spontaneous seizures, machine-based algorithms were trained to detect "taggable" features of tonic clonic seizures, such as loss of righting reflex**. Loss of righting reflex, a reliable feature of loss of consciousness in mice, occurs consistently during spontaneous seizure.

Here we describe the development of the machine learning technology, and the application in spontaneous seizure monitoring and multiplexing other phenotypic readouts (activity, sleep wake cycle, etc.).

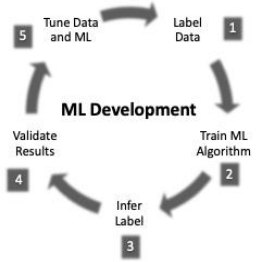
Introduction

What are the taggable behaviors associated with seizure in mice?



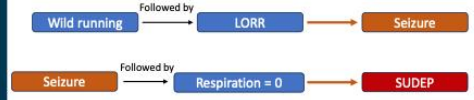
Loss of Righting Reflex (LORR): loss of ability to maintain upright body posture; means of detecting loss of consciousness associated with seizure

This work covers the development of LORR biomarker



Digital Biomarker development is an iterative process between biologists and machine learning scientists.

Future work will combine LORR with other metrics to create seizure and SUDEP biomarkers

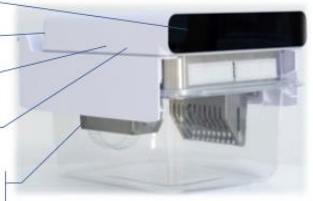


Enabling Technology

Digital home-cages allow for 24/7 recording and behavioral analysis with cloud based digital biomarkers

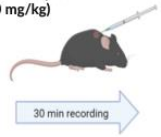
Individualized animal behavior data enabled by specialized ear tags

- Digital Cage Card
- Single-board computer
- Two HDR Cameras
- Integrated IR and VIS lighting
- Integrated water bottles, food hopper, and running wheels



Inducible seizure assay (PTZ) to generate annotated dataset for LORR biomarker training

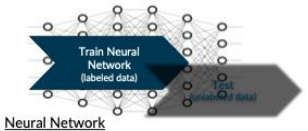
S.C. PTZ injection (80 mg/kg)



Inducible PTZ seizure assay in WT C57BL6/J mice recorded behavior mice in digital cages for 30 mins.

1 Manual Annotation of Loss of Righting Reflex (LORR)

Manual Selection of Labeled Frames



Neural Network

Pros:
- Preserves information from original data
- No need to manually define heuristics

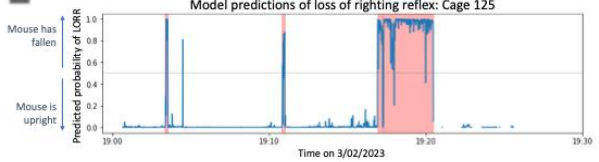
Cons:
- Not explainable

Assess LORR results on video data from PTZ assay and SCN1A natural history study

PTZ Video

3

Red shading : BioMarin's labeled LORRs



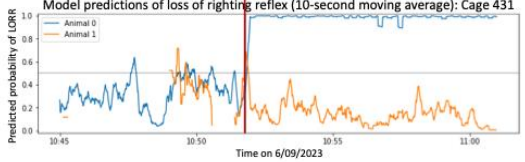
4 Model trained on PTZ-data (tested on PTZ data)

	Predicted non-LORR	Predicted LORR
True non-LORR	188	9
True LORR	7	172

96% of true LORR samples are identified by the model
5% of LORR detections are false positives

SCN1A Video

Annotation on app: hindlimb extension, SUDEP



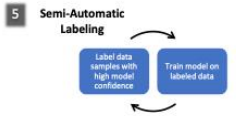
Model trained on PTZ-data (tested on SCN1A data)

	Predicted non-LORR	Predicted LORR
True non-LORR	2108	177
True LORR	152	42

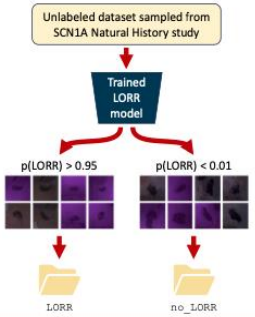
22% of true LORR samples are identified by the model
80% of LORR detections are false positives

Increase labeled training dataset to tune LORR performance

5 Semi-Automatic Labeling



Model performance was low in conditions the model hadn't been trained in, such as:



Improved Model Performance:

Model trained on PTZ & SCN1A data (tested on SCN1A data)

	Predicted non-LORR	Predicted LORR
True non-LORR	2770	68
True LORR	231	272

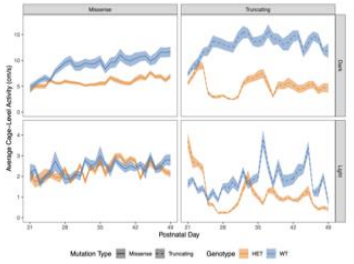
- **54%** of true LORR samples are identified by the model
- **20%** of LORR detections are false positives

Additional rounds of training necessary to increase the recall and precision of our LORR model

SCN1A Natural History Dataset highlights digital biomarker creation, application and discovery process

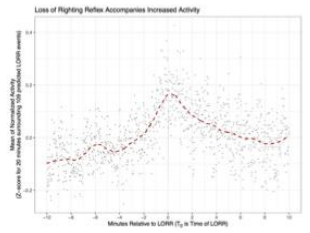
N=65 mice total (~15 per genotype/ strain) weaned 1-3 mice/cage at P21, recorded until P50

Application: multiplex phenotypic readouts-- locomotion data illustrates hypoactivity of SCN1A Hets vs WT mice in dark cycle

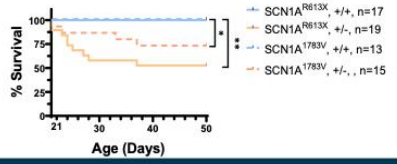


Biomarker discovery can be strengthened and tuned by incorporating data mining techniques

Shown to the right, LORR predictions from SCN1A dataset are often accompanied by increased locomotion, presumed to be "wild running"



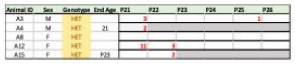
Creation: SUDEP Phenotype can be used as substrate for future biomarker development



STARTING POINT
Manual

Watched 288 hours of video at x8 speed to detect 28 seizures in 4 HET mice (36 human hours, approx. 1 work week)

Labor intensive and low-throughput



WE ARE HERE
Semi-Automated

Use LORR model predictions to screen spontaneous seizures in video

- 89% of manually detected seizures are detected by LORR
- 100+ spontaneous tonic clonic seizures detected as of November 2023 (analysis ongoing)

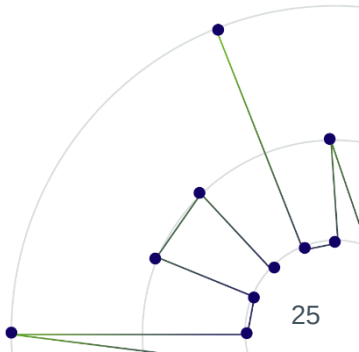
COMING SOON
Fully Automated

- Combine LORR model with other taggable seizure behaviors to increase specificity of biomarker
- 24/7 live individual animal seizure monitoring in group housed home-cage system
- Ability to answer complex biological questions on how spontaneous seizure interplays with other disease phenotypes in SCN1A natural history study and in other preclinical epilepsy models

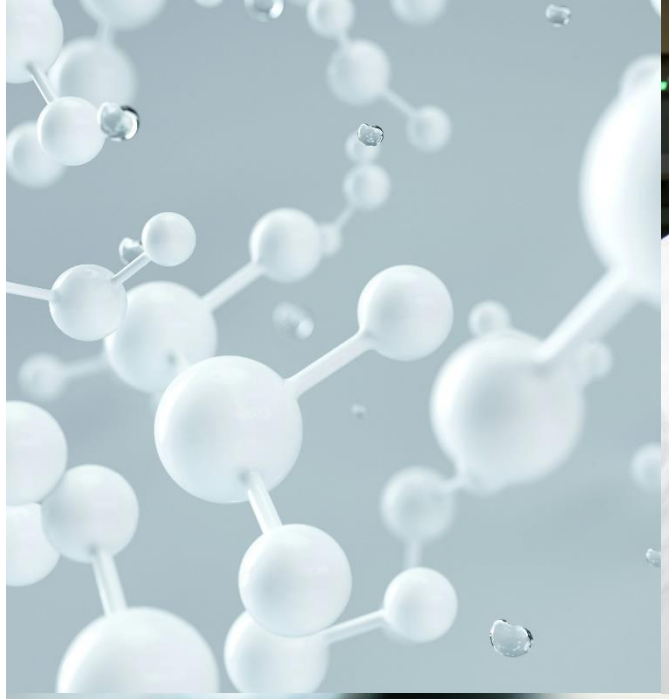
Digital In Vivo Alliance members work together non-competitively for the purpose of exploring preclinical applications of AI-enabled digital biomarkers from home cage-compatible technologies. For more information, visit DIVA.bio

What’s next in AI?

- Chart redacted for copyright.
- Chart available here: https://ourworldindata.org/grapher/test-scores-ai-capabilities-relative-human-performance

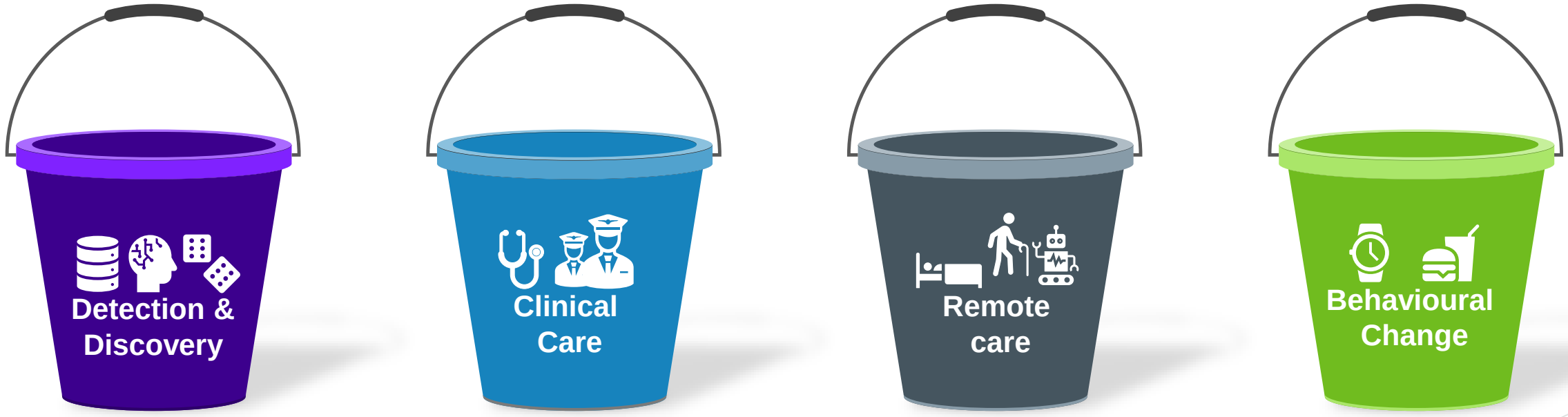


Healthcare advancements watchlist



CLUB VITA

How might “AI” impact healthcare & longevity?

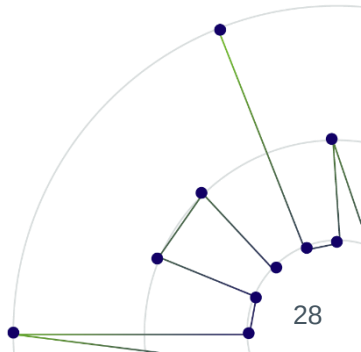


We want to hear from you!

Periodical Survey

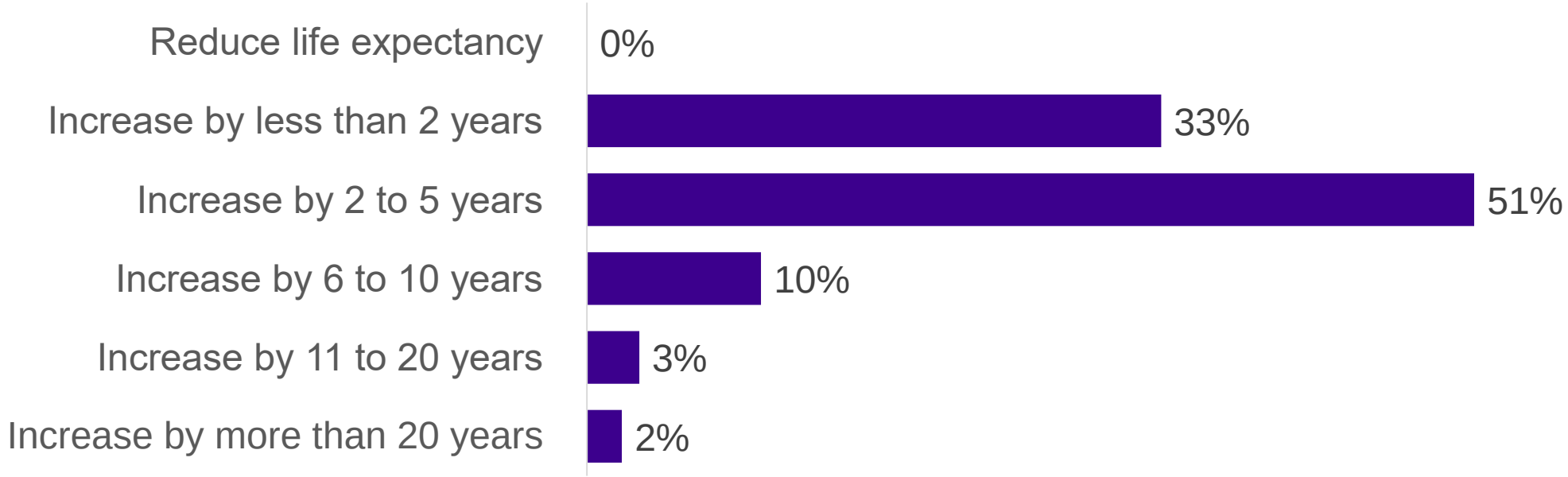
What are your views on promising areas of research, views on future life expectancies and lifespan?

- First of a regular survey
- Aim to track trend in outlook on longevity
- Results shared with participants
- Look out for details in inbox!



Poll question

"How will big data and AI contribute to changes in life expectancy for a 60-year-old in 20 years' time?"



CLUB VITA and Nationwide

THE RISK OF **LIVING LONGER**

Douglas and Uli ask the ultimate question of human longevity for financial institutions:

How long can we go?

Series program

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Session 2 May 7th, 2024	*The biology of aging*	• Richard Faragher, University of Brighton • Niharika Duggal, University of Birmingham	Recording here
Session 3 May 28th, 2024	*Cancer research*	• Gao Xiao, SCOR • Catherine Pickworth, Cancer Research UK	Recording here
Session 4 June 18th, 2024	*Biological clocks*	• Peter Joshi, Humanity Inc • John Schoonbee, Swiss Re	Recording here
Session 5 July 9th, 2024	*Using Big Data and AI to improve and advance longevity*	• Gregg TeHennepe, The Jackson Laboratory • Steven Baxter, Club Vita	Today!
Session 6+ Stay tuned!	More sessions will be added in fall 2024 Reach out with your suggested topics!		

For full details and registration for the series,

CLUB VITA visit: www.clubvita.net/uk/events or follow http://linkedin.com/company/club-vita

Thank you