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?

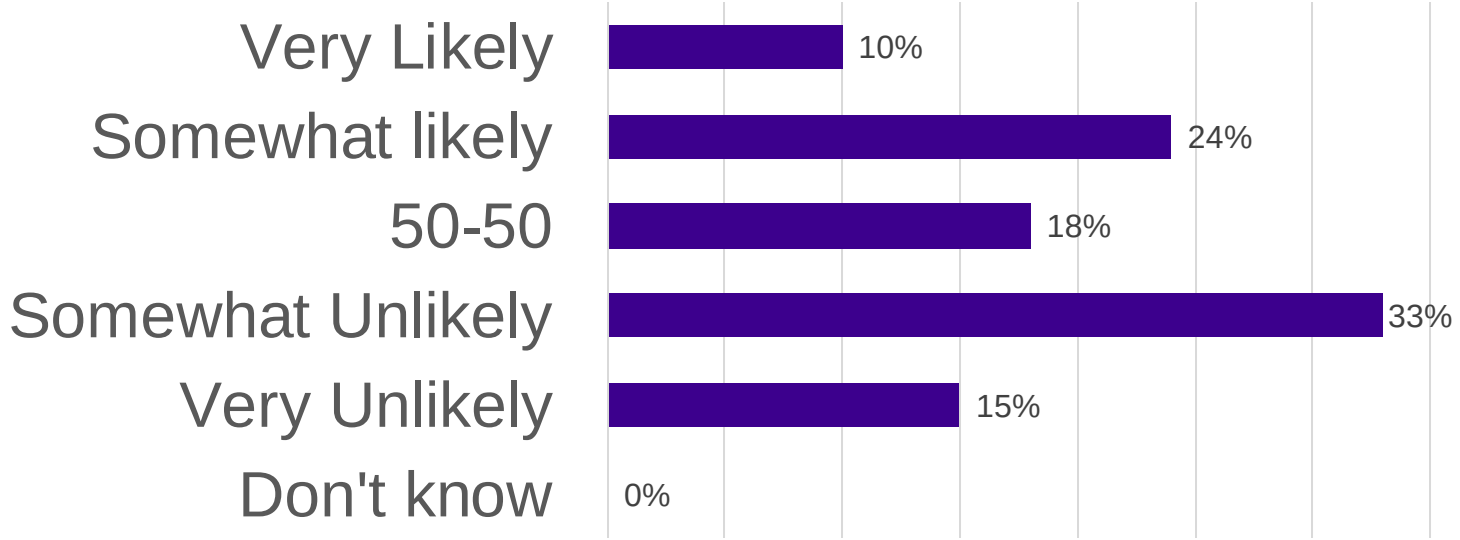
Series program

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	Today!
Session 2 May 7th, 2024	*The biology of aging*	• Richard Faragher, University of Brighton	Register here
Session 3 May 28th, 2024	*Cancer research*	• Xiao Gao, SCOR • Catherine Pickworth, Cancer Research UK	Register here
Session 4 June 18th, 2024	*Biological clocks*	• Peter Joshi, Humanity Inc	Register here
Session 5 July 9th, 2024	*Using AI to improve and advance healthcare*	• tbc	Register here

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

Poll question

"How likely is it that annual mortality improvements will increase materially above the levels we saw in the c100 years up to 2019 in the next 20-30 years?"



An introduction to the question of human longevity: *How long can we go?*

Douglas Anderson
(Chair)
Founder & Chief Visionary Officer, Club Vita

Ulrich Stengele
(Chair)
Chief Actuary, Nationwide Financial

Dan Ryan

Director of Demographic Risk, Just Group

Phil Newman

CEO & Founder, Longevity.Technology

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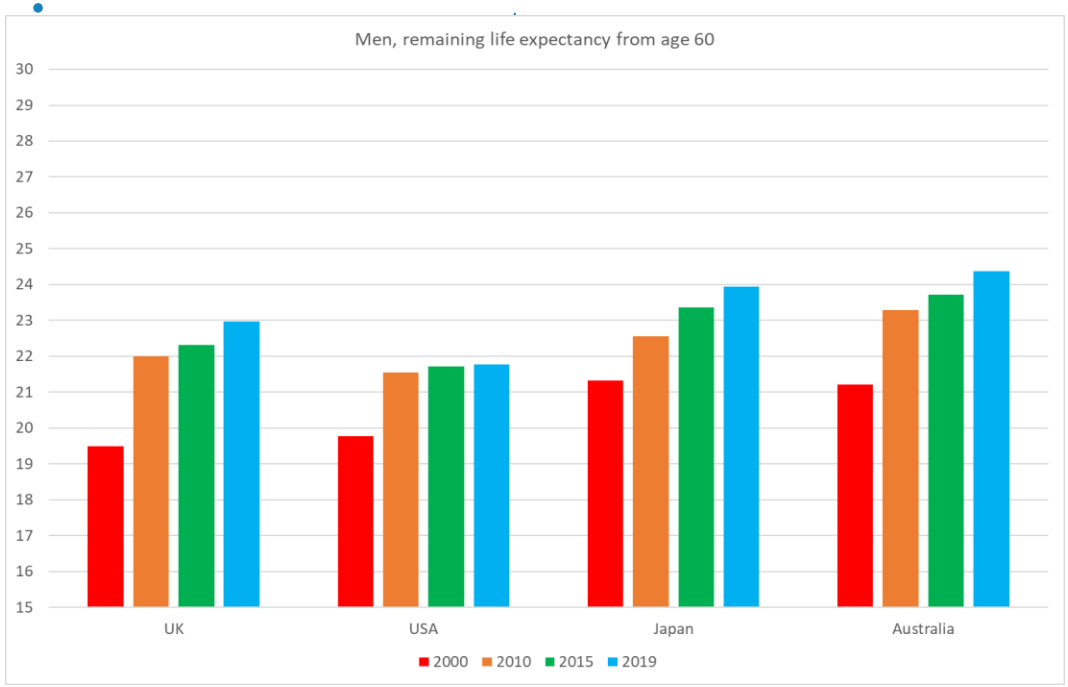
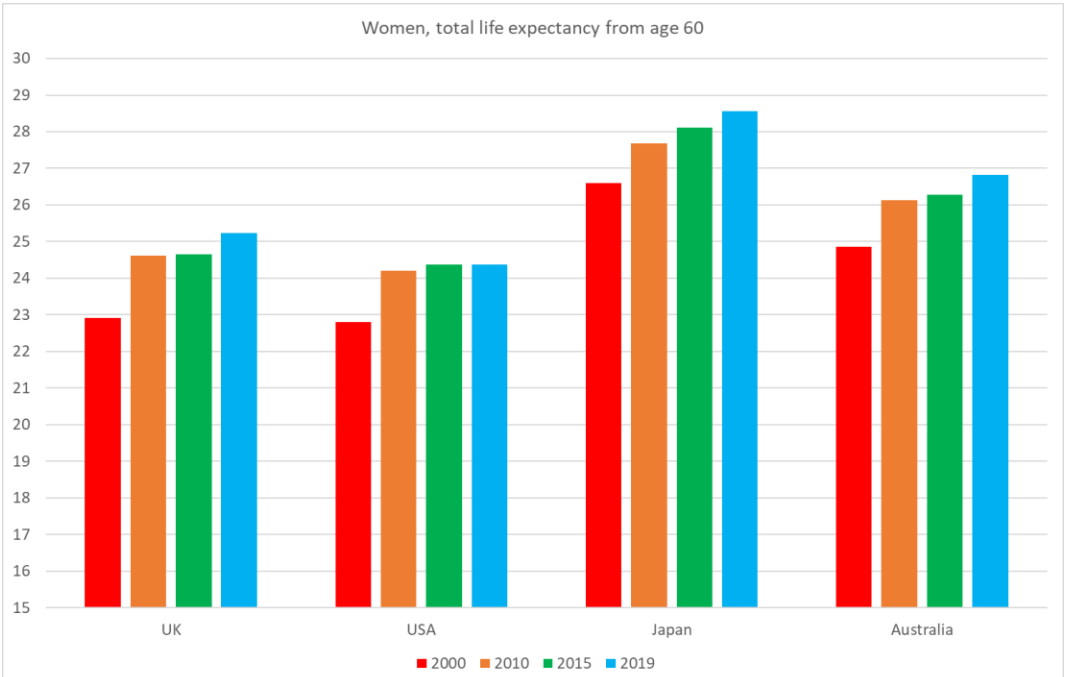
Looking back at historical pace of mortality improvements





Men – Annual increase in life expectancy from age 60

	2000-2010	2010-2015	2015-2019
UK	0.25	0.06	0.16
USA	0.18	0.04	0.02
Japan	0.12	0.16	0.15
Australia	0.21	0.09	0.16

Women – Annual increase in life expectancy from age 60

	2000-2010	2010-2015	2015-2019
UK	0.17	0.01	0.15
USA	0.14	0.03	0.00
Japan	0.11	0.09	0.11
Australia	0.13	0.03	0.14

Source: Global Health Observatory

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How actuaries have attempted to predict the future

Extrapolative

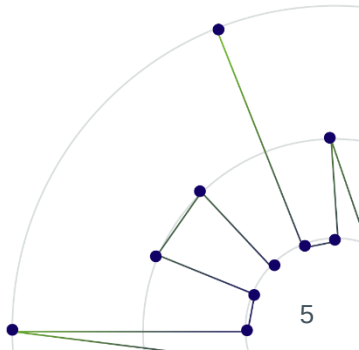
- Forecast using time series extrapolation
- Strong probabilistic framework, but relies on past data

Expectation

- Forecasts / scenarios based on expert opinion
- Simple, not limited to past data, but subjective and deterministic

Explanative

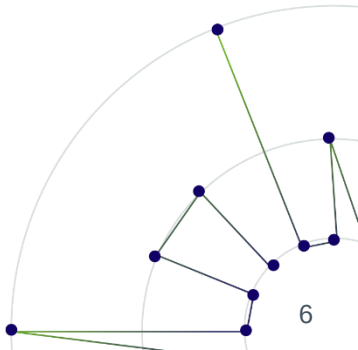
- Understand the past and use it to model the future
- Base on structural or causal epidemiological models



Pre-pandemic predictions produced by GBD (central)

Chart redacted for copyright.

- Chart available on p2079 of Forecasting life expectancy, years of life lost, and all cause and cause-specific mortality



Pre-pandemic predictions produced by GBD (optimistic)

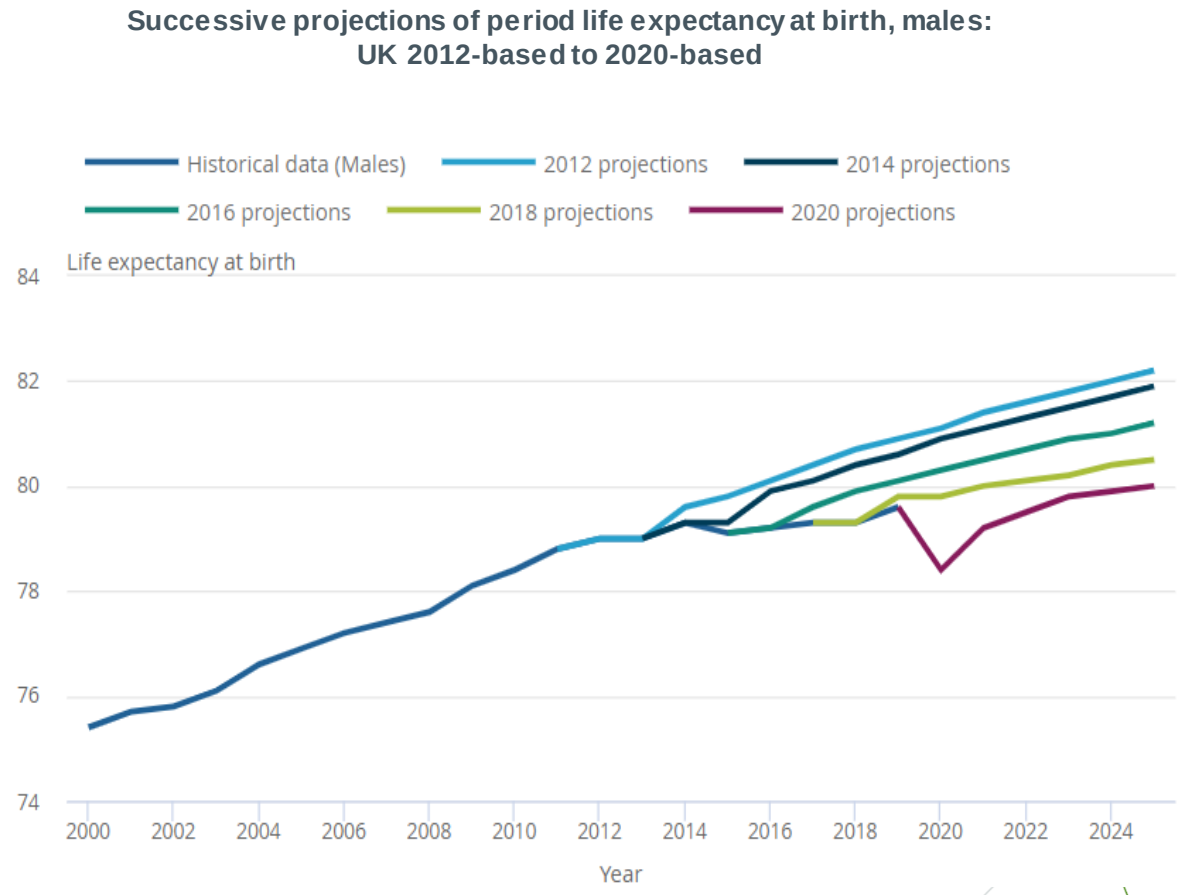
Chart redacted for copyright.

- Chart available on p2079 of Forecasting life expectancy, years of life lost, and all cause and cause-specific mortality

Decades of challenging predictions - back to the drawing board?

Chart redacted for copyright.

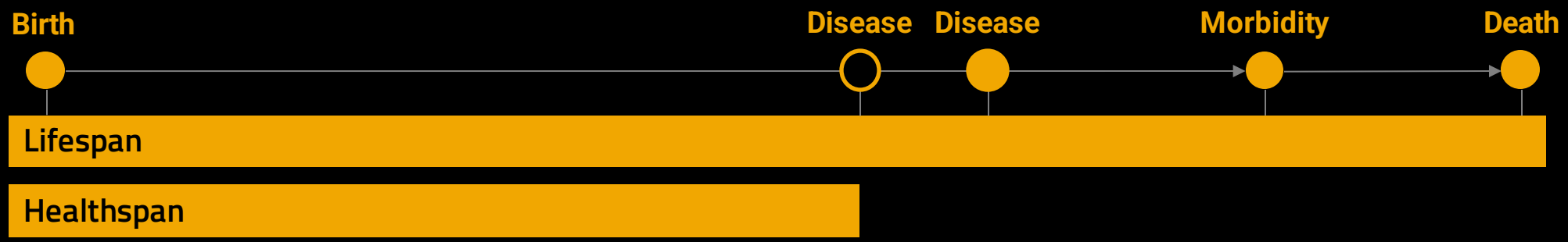
- Chart available on p13 of the ONS's National Population Projections Accuracy Report, 2016



Source: National population projections, mortality assumptions: 2020- based interim

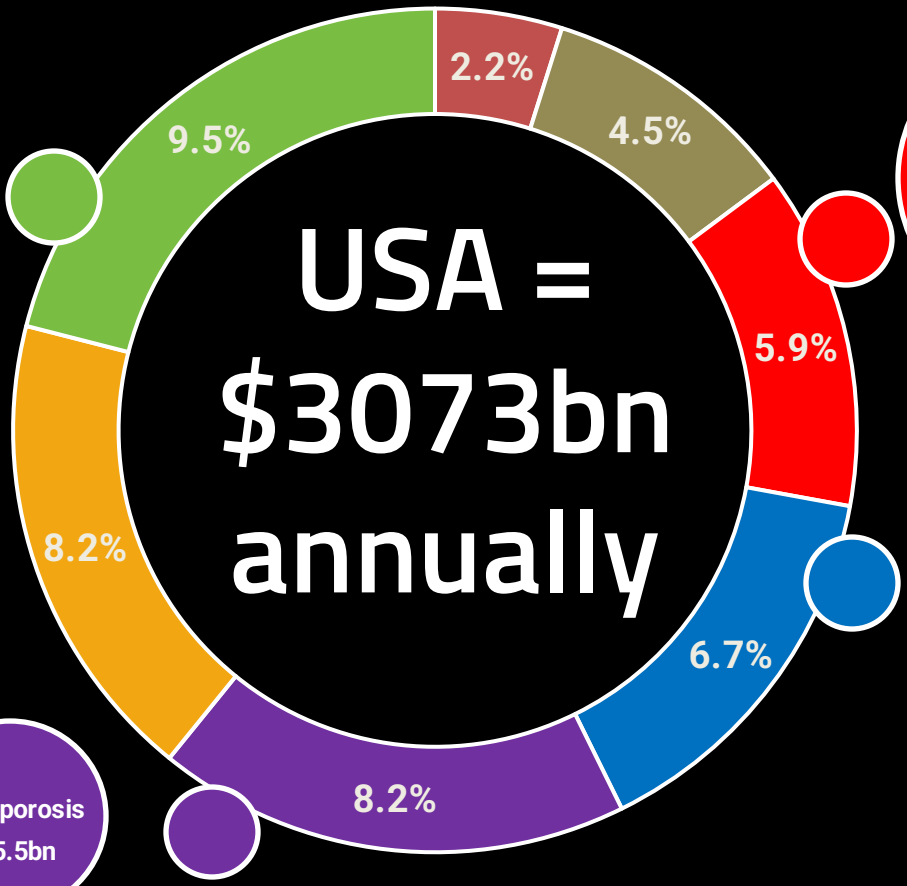
What is longevity?

Early detection and intervention targeting the pathways and diseases of aging ...



... leading to extended healthspans, longer and more productive lives:

Aging diseases cost a lot!



Heart Disease $219bn

Hypertension $198bn

Stroke $53bn

Osteoarthritis $65bn

Osteoporosis $25.5bn

Obesity $173bn

Type 2 Diabetes $363bn

Alzheimer's Disease $305bn

Parkinson's Disease $52bn

AMD $3.5bn

Defining longevity: Domains

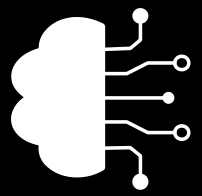

Seno-therapeutics

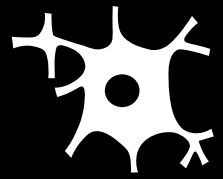

Longevity supplements


Young blood

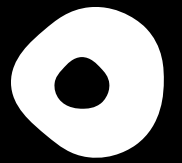

Longevity diagnostics

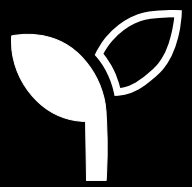

Aging in place


Neurotech


Longevity immunity


Discovery platforms


Rejuvenation


Regeneration

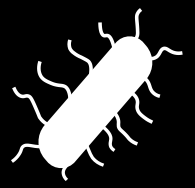

Cellular Re-programming


Metabolic rejuvenation


Companion longevity


Advanced aesthetics


Repurposed drugs


Microbiome


Longevity genetics


Longevity platforms

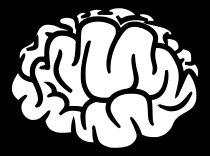

Longevity lifestyle


Longevity clinics


Longevity drugs


Functional food

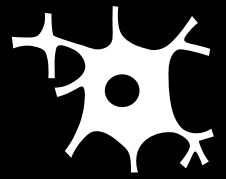

Education


Neuropharma


Reproductive longevity

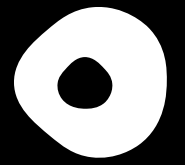
Defining longevity: Domains: Longevity Biotech

Seno-therapeutics

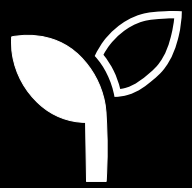


Longevity immunity

Discovery platforms



Rejuvenation



Regeneration

Cellular Re-programming

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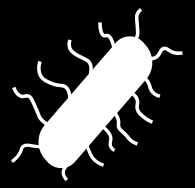
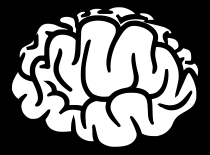
Repurposed drugs



Microbiome

Longevity genetics

Longevity drugs



Neuropharma

Reproductive longevity

Is it here already?

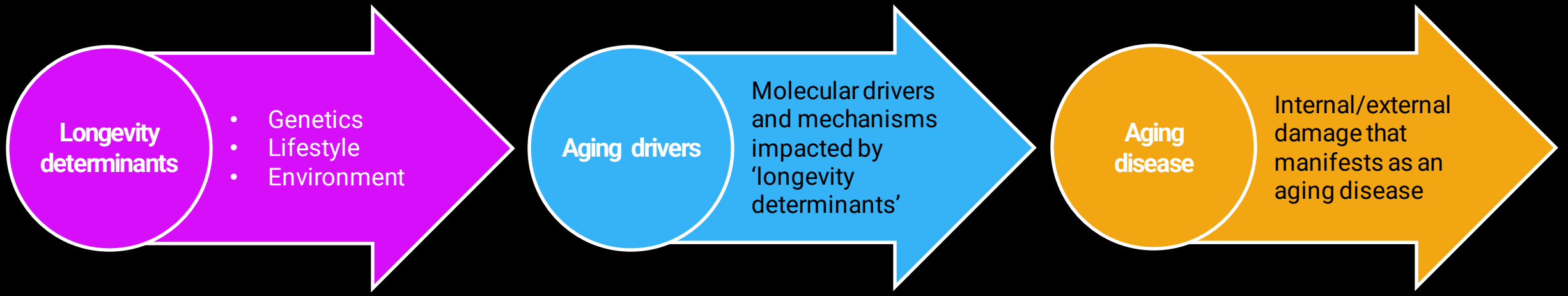
Longevity now

- Digital apps
- Clinical services
- Biomarkers
- CROs
- Supplements
- + others

Longevity next

- Drug discovery
- Repurposing
- Reprogramming
- Supplements
- Gene therapies
- + others

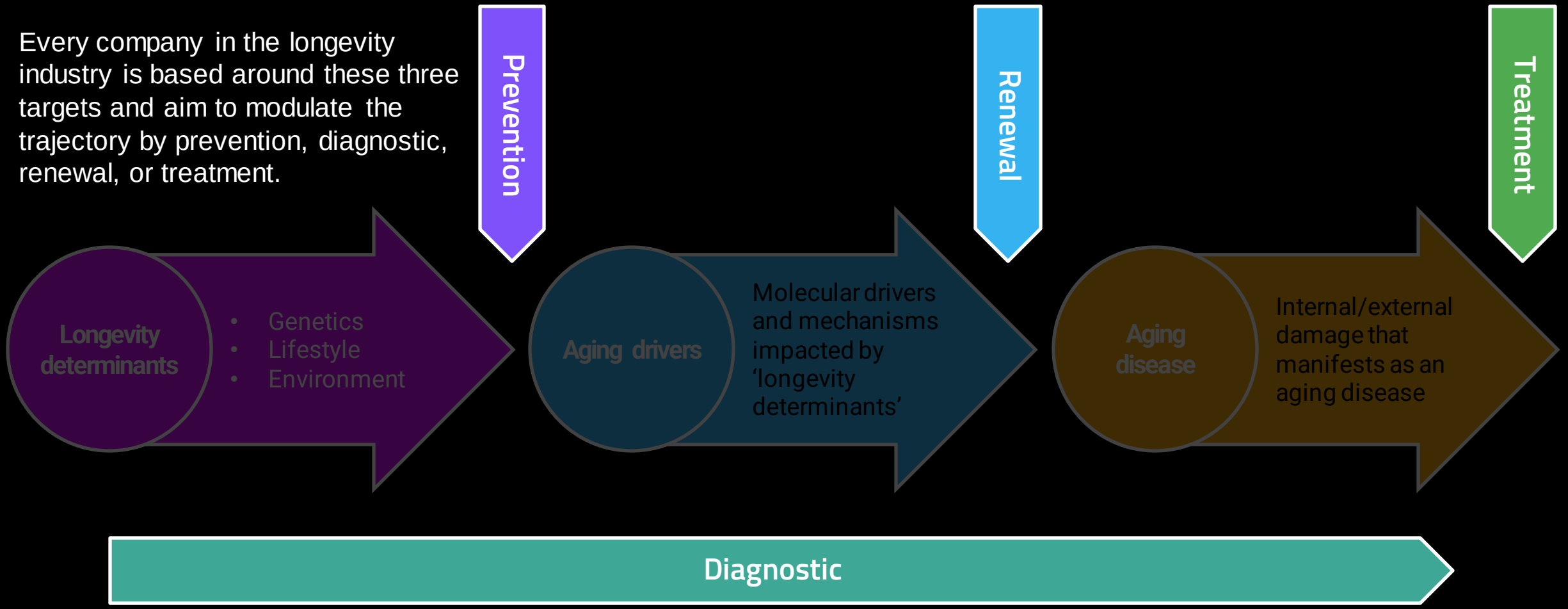
Defining longevity: 3 Targets



Aging pathways, mechanisms and hallmarks					
Epigenetics	Mitochondrial dysfunction	Immuno-modulation	IGF-1	Nf-Kb	Nrf3
DNA repair	Progeronic chronokines	Reproduction	Insulin	IL-1B	PAI
Telomere regulation	Oxidative stress	Glycation	mTOR	P53	Wnt
Proteostasis	Stem cell exhaustion	Defective autophagy	FOXO	Ang-II	SIRTs
Nutrient sensing	Cellular senescence	Androgenic signalling	AMPK	AKT	NAD
Macromolecular damage	Dysregulated microbiome				

Defining longevity: 4 pillars

Every company in the longevity industry is based around these three targets and aim to modulate the trajectory by prevention, diagnostic, renewal, or treatment.



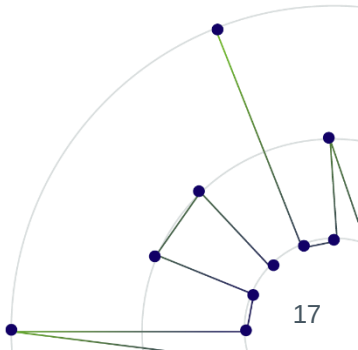
Example applied to CVD

	Prevention	Diagnostics	Renewal	Treatment
	Prevent damage that accelerates aging and modify longevity determinants and aging drivers.	Early identification of health status and accumulation of aging damage. Diagnostics span across longevity determinants, aging drivers and at the point of aging disease.	Reversal of damage that has occurred. This includes either accumulated damage before disease has arisen, damage arising from aging drivers, or that which occurs at the point of disease.	Treatment of damage that has occurred. This means direct treatment of an aging disease.
Current approach	Prescription medications	ECG, EGG	Pacemaker, lipid-lowering agents	Angioplasty/stents, bypass surgery
Longevity approach	Exercise, Mediterranean diet, longevity supplements	Epigenetic clock to predict CVH (BASE-II)	Treatment of atherosclerosis-related risk (by removal of arterial plaque)	Heart repair by cardiac reprogramming

Smoking – putting behavioural change in the limelight

Charts redacted for copyright.

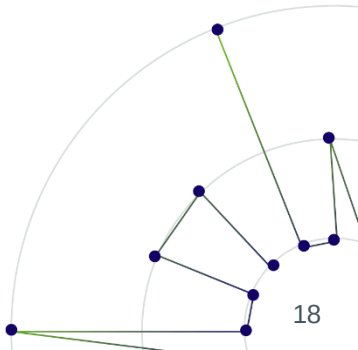
- Charts available on p5 of the 50 years of follow-up on British Doctor Study



Potential for healthy lifestyles to increase life expectancy

Chart redacted for copyright.

- Chart available on p14 of the Impact of Healthy Lifestyle Factors on Life Expectancies in the US population



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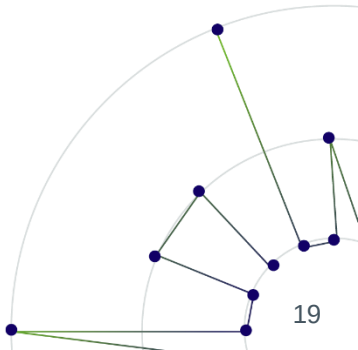

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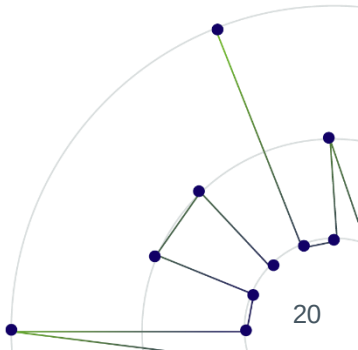
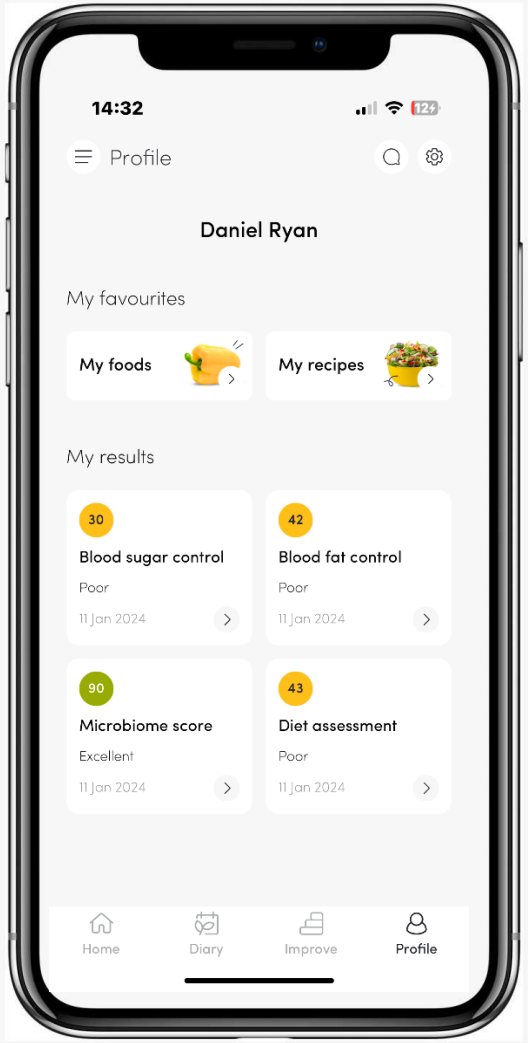
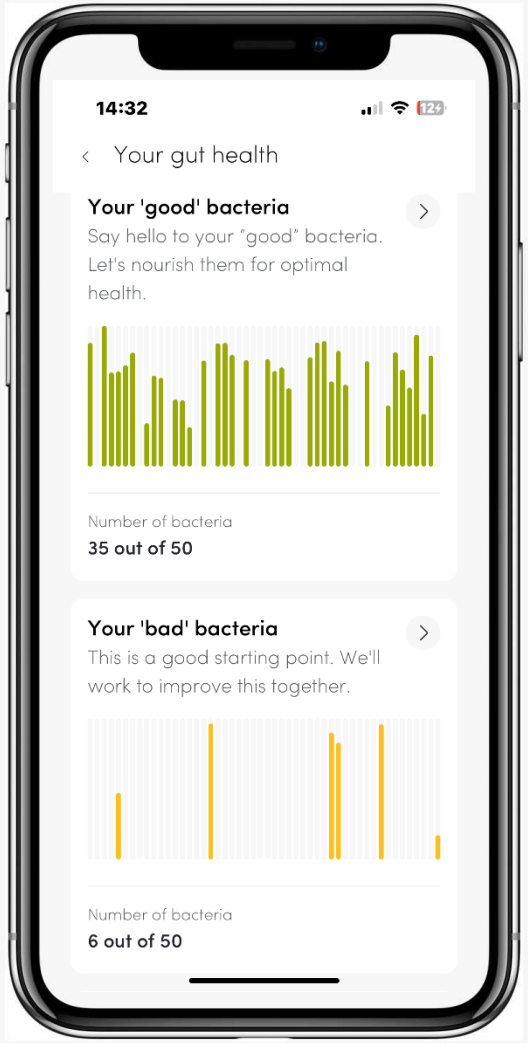
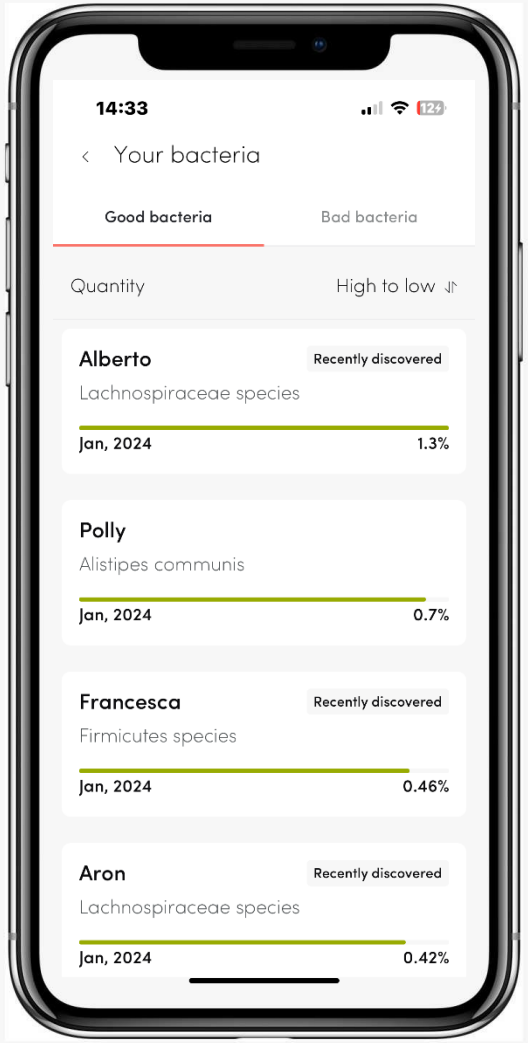
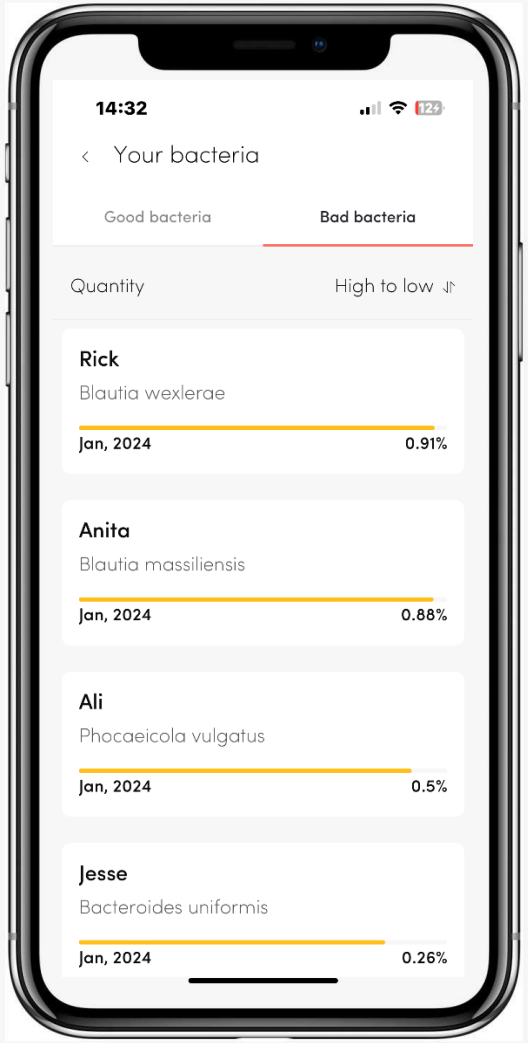


Power of the crowd to drive insights & improvements - ZOE









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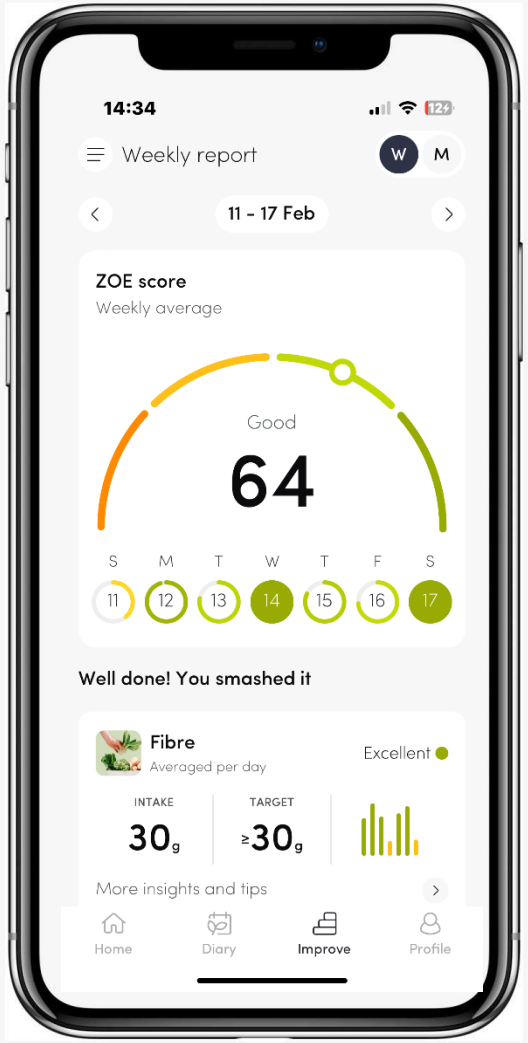
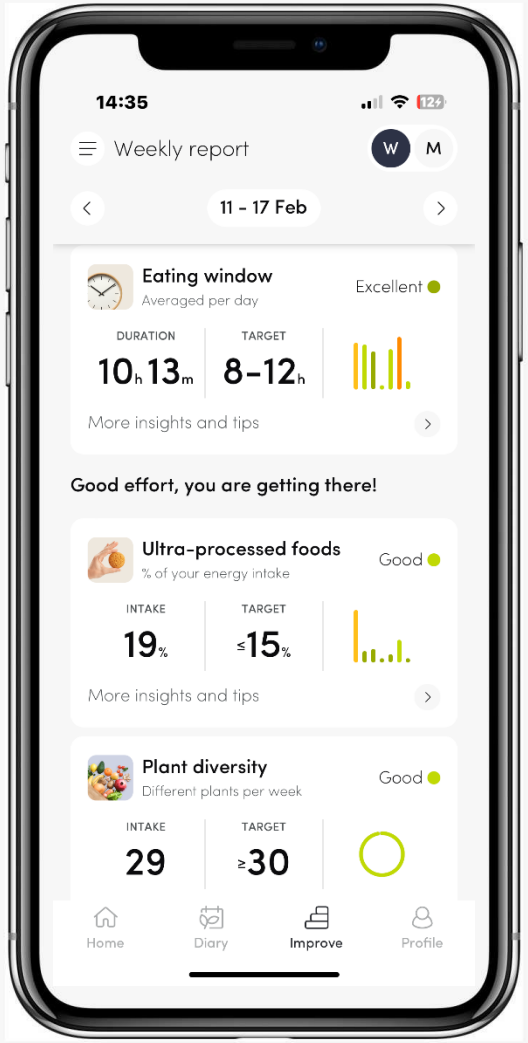
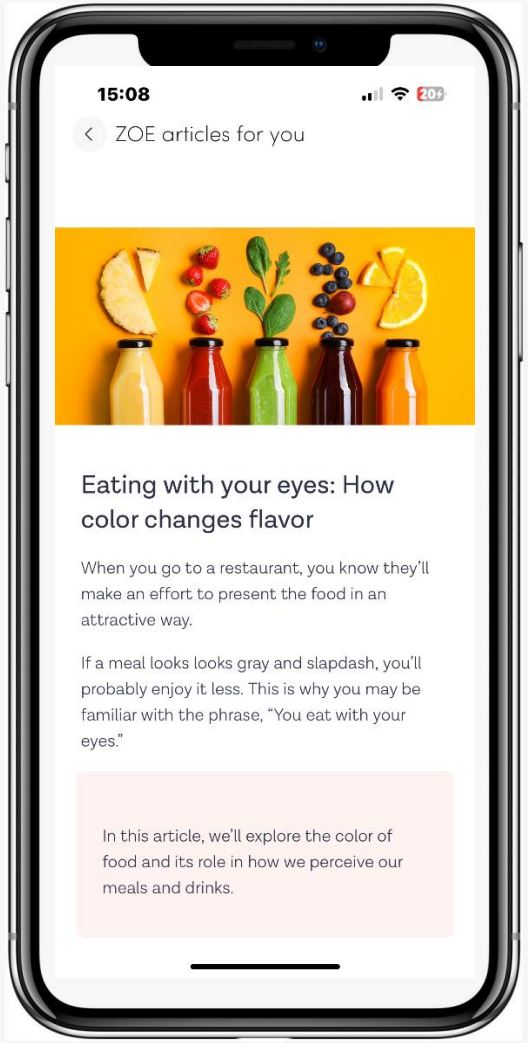
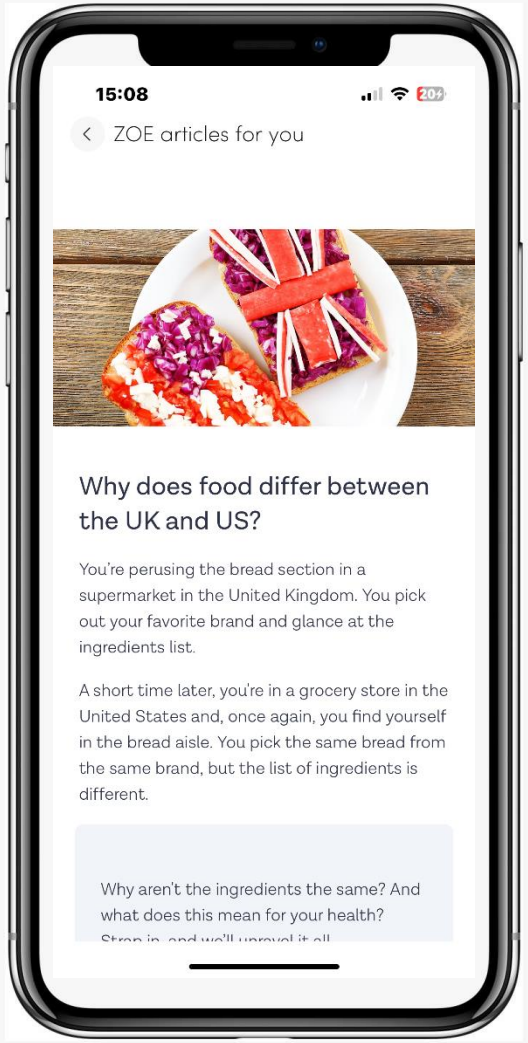
Power of the crowd to drive insights & improvements - ZOE





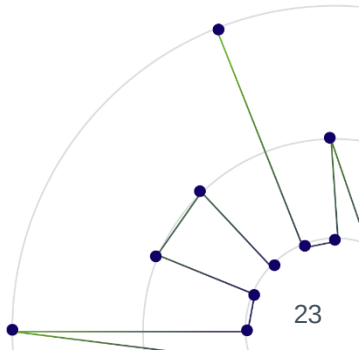




Using machine learning to classify within populations
Life2Vec trained on Danish national population

Chart redacted for copyright.

- Chart available as fig 1 in Nature Computational Science's A transformer method that predicts human lives from sequences of life events



A landscape of future drivers of life expectancy

Chart redacted for copyright.

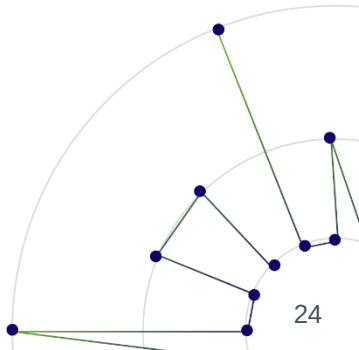
- Chart available on p15 in Swiss Re's The future of life expectancy, 2023

Questions to ask?

How likely?

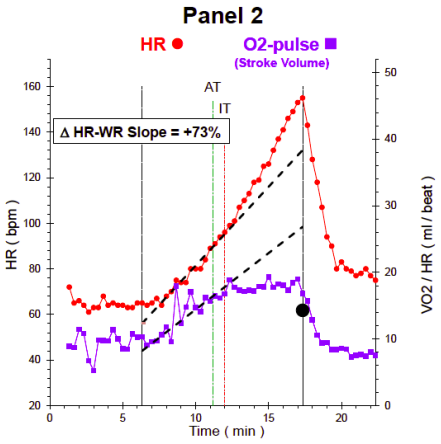
Peak impact?

When and where available?



My experience as a 1% (er)

Healthy Longevity Center, Florida



EKG Summary: Abnormal ST depression without ventricular ectopy

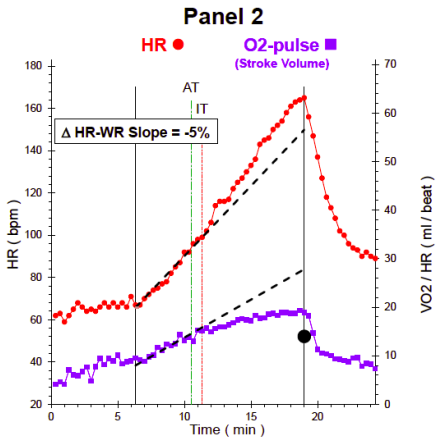
Functional Capacity:
- Peak VO2 = 121% of predicted.

Cardiovascular Risk Assessment: INCREASED - Yellow*
- HR@IT = 96 beats per minute

Target Peak VO2: 40 ml/kg/min**

* See Risk Stratification and Management Page
** 10% Increase from Baseline

23 March 2023



EKG Summary: Abnormal ST depression without ventricular ectopy

Functional Capacity:
- Peak VO2 = 140% of predicted.

Cardiovascular Risk Assessment: INCREASED - Yellow*
- HR@IT = 100 beats per minute

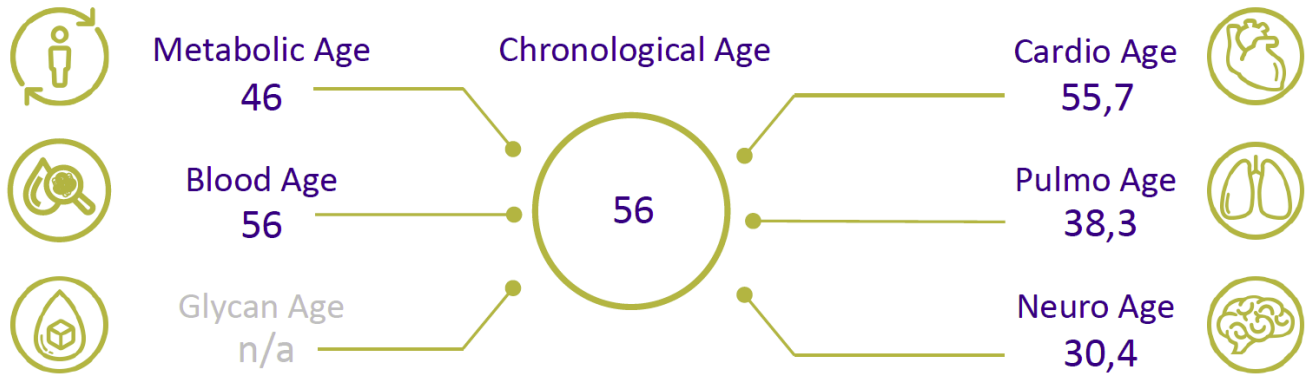
Target Peak VO2: 46 ml/kg/min**

* See Risk Stratification and Management Page
** 10% Increase from Baseline

14 November 2023

My experience as a 1% (er)

Longevity Center, Warsaw



24 October 2023

Patient Profile	Percentile Range				> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range				> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Patient Score	Standard Score	Percentile	VI**	Above	Average	Low Average	Low	Very Low
Neurocognition Index (NCI)	NA	105	63	Yes		X			
Composite Memory	99	104	61	Yes		X			
Verbal Memory	49	90	25	Yes		X			
Visual Memory	50	116	86	Yes	X				
Psychomotor Speed	202	133	99	Yes	X				
Reaction Time*	828	75	5	Yes				X	
Complex Attention*	4	108	70	Yes		X			
Cognitive Flexibility	48	106	66	Yes		X			
Processing Speed	63	123	94	Yes	X				
Executive Function	49	106	66	Yes		X			
Working Memory	12	111	77	Yes	X				
Sustained Attention	34	113	81	Yes	X				
Simple Attention	40	107	68	Yes		X			
Motor Speed	138	129	97	Yes	X				

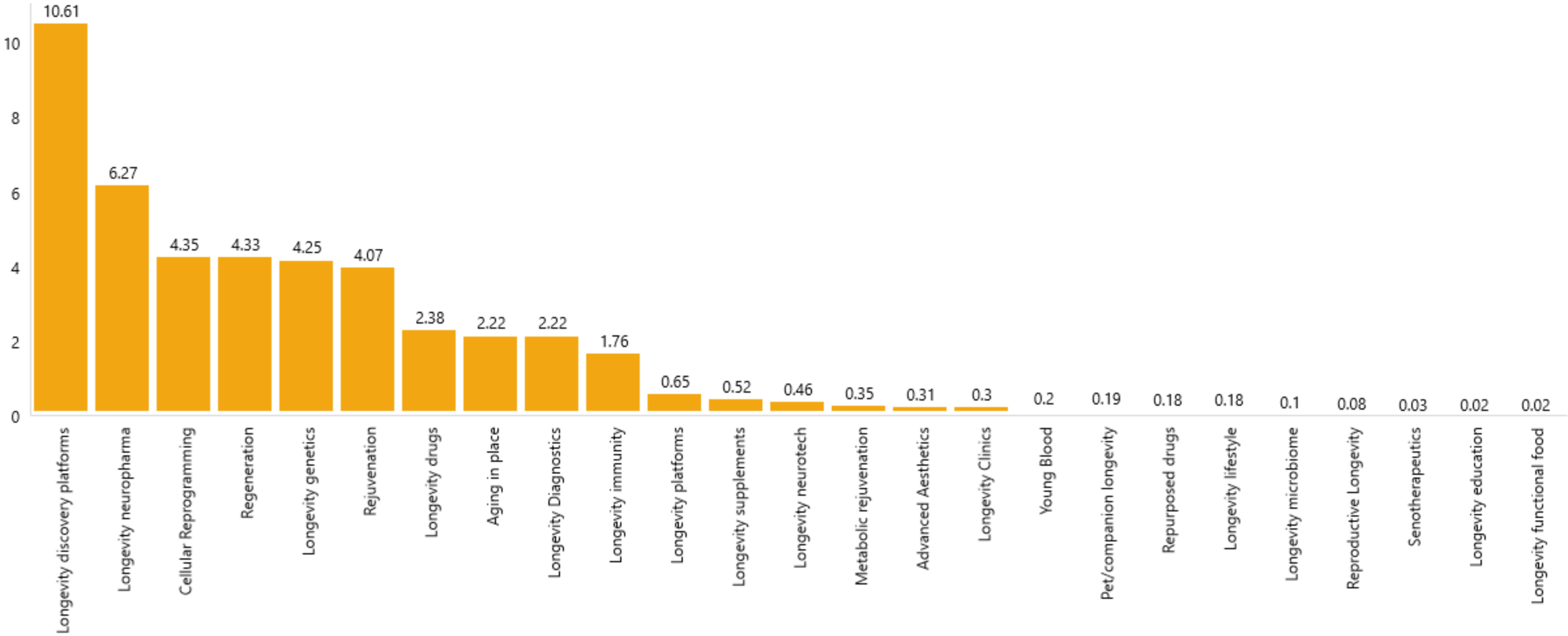
24 October 2023

Overall progress by longevity biotech domain

	Pre	1	2	3	App
Cellular reprogramming					
Discovery platforms					
Longevity drugs					
Longevity genetics					
Longevity immunity					
Microbiome					
Neuropharma					
Metabolic rejuvenation					
Regeneration					
Rejuvenation					
Reproductive longevity					
Repurposed drugs					
Senotherapeutics					

Figure: Longevity companies investment activity analysis by Longevity.Technology, based on Pitchbook data funding data as of 31/12/23.

Total financing ($bn) by domain over the last 5 years



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Overall progress by longevity biotech domain

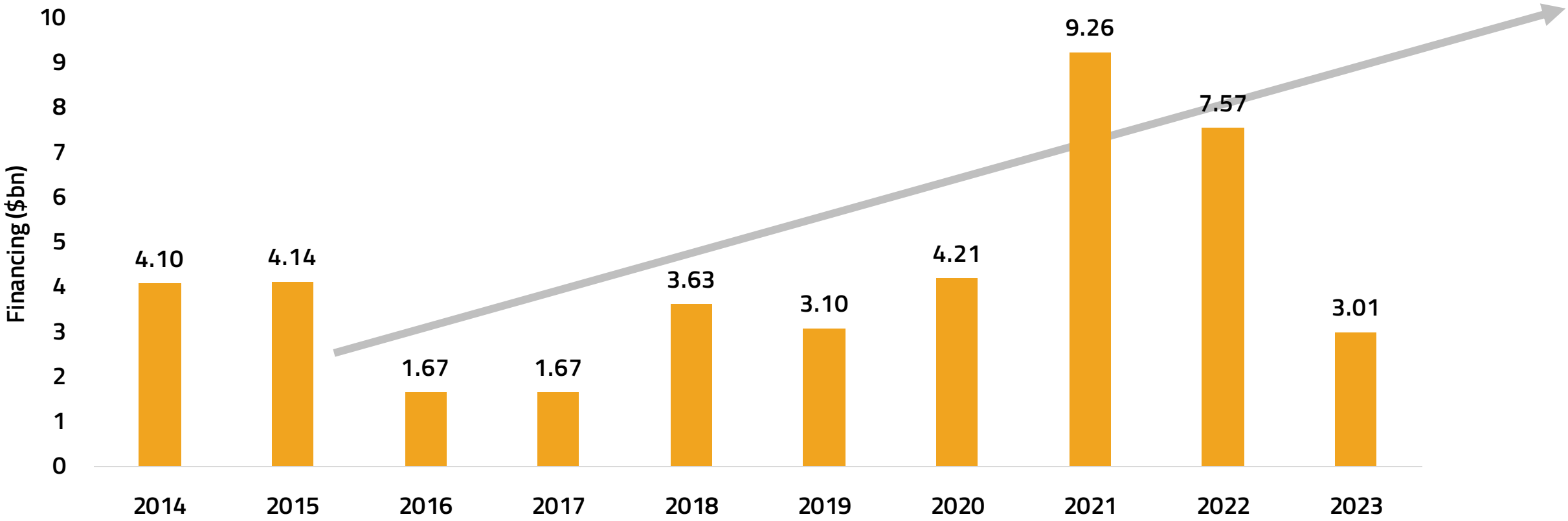


Figure: Longevity companies investment activity analysis by Longevity.Technology, based on Pitchbook data funding data as of 31/12/23.

Widening differences in life expectancy

UK

Chart redacted for copyright.

- Chart available as fig 4 in The King's Fund

USA

Chart redacted for copyright.

- Chart available as fig 4 in The Washington Post

Continuing impact of COVID-19 on survivors

Complement activation

Reduced cortisol

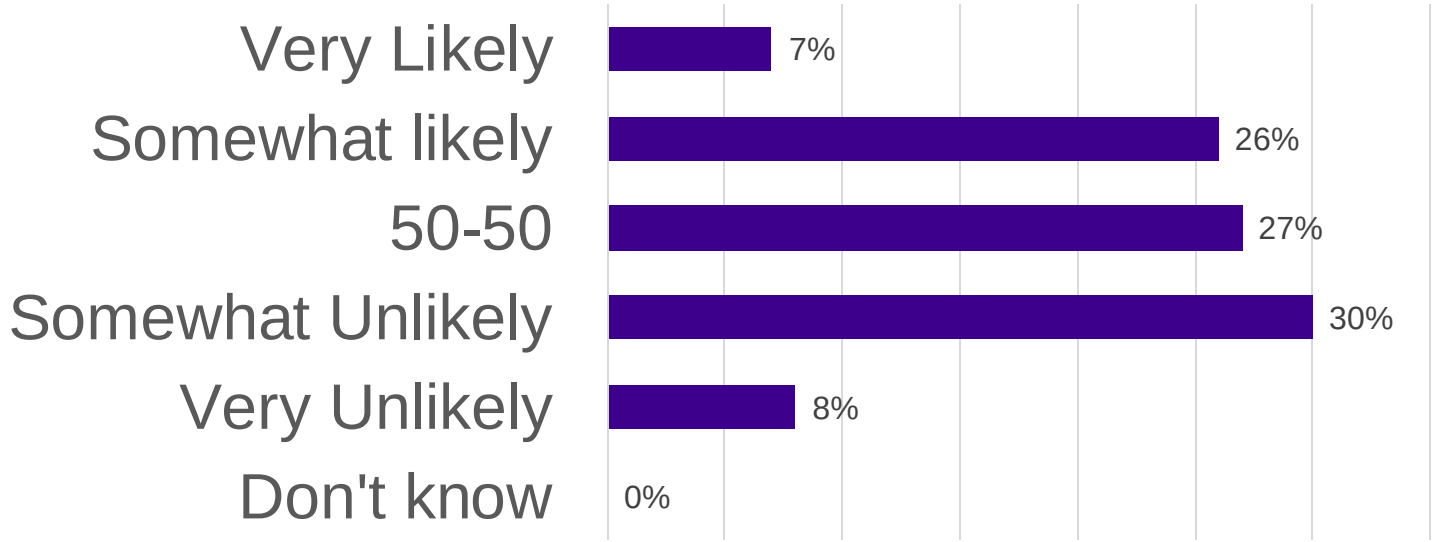
Serotonin depletion

Chart redacted for copyright.

- Chart available as fig 3 in Cognition and Memory after COVID-19 in a Large Community Saumple

Poll question

"How likely is it that annual mortality improvements will increase materially above the levels we saw in the c100 years up to 2019 in the next 20-30 years?"



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

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	Today!
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Session 5 July 9th, 2024	*Using AI to improve and advance healthcare*	• tbc	Register here

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Thank you