

Welcome!

@ClubVita
#longevityblackswans

Longevity Black Swans

Guy Coughlan, Chief Risk Officer, Universities Superannuation Scheme

Paul Kitson, Partner, PWC

Douglas Anderson, Founder of Club Vita

24 April 2018

In the pipeline...

The sugar tax is nearly here



Erik Pickett • Manager
Actuary at Club Vita

The beginning of the new tax year means the much anticipated sugar tax on sweet drinks is nearly here. But, will this have a positive effect on the populations health?



Sugar tax is already producing results

A levy on sugary drinks will not raise as much as thought because makers are changing their recipes.

"As with controls on tobacco, I think we will look back and wonder why we did not do this sooner."

"It will be interesting to see how much sugar intake falls as a result of the tax and the recipe changes already underway. Perhaps we also consider a Salt Tax as well?"

"...In Mexico, tax on sugar-sweetened beverages was associated with a decline in purchases over a study period of two years with no evidence of health effect over time."

Socioeconomic



Nicola Oliver
Longevity, Mortality & Morbidity Consultant at Medical Intelligence

disparities in first stroke incidence

Patients from the most deprived areas had an age of stroke onset 7 years younger than those in the least deprived areas.

"Let's hope that it leads to more effective health interventions to change the unhealthy habits of the less affluent."

Top charts 2 – 2017 deaths



Conor O'Reilly
Longevity consultant at Club Vita

Issue 2 of Club Vita's "Top Charts" series is now out. It compares population average deaths per week in 2017 to previous years (spoiler – it's higher!)

Club Vita asks: How does the number of deaths in England & Wales over 2017 compare to previous years?

Unlike Comment | You + 10 4

It's not every day actuarial mathematics makes the mainstream news



Elaine Murphy
Consulting Actuary at Hyman Robertson

18yr old lottery winner chooses \$1,000 a week for life over \$1,000,000 lump sum, did she choose wisely?



Lottery win teen: Did she choose wisely?

Charlie Lagarde took C\$1,000 a week for life, rather than a C\$1m lump sum, after winning a lottery.

"Couldn't resist getting my calculator out... assuming a 3% interest rate she wins (again) if she lives much past 47."

"...her income level could be in the top quartile and her life expectancy would be higher than quoted age of 82... plus Quebecers currently have the highest level of mortality improvements compared to the rest of Canada."

Welcome



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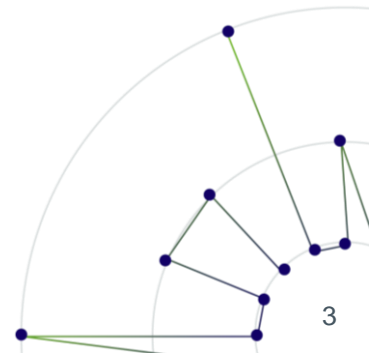
@pensionkit



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Twitter: @ClubVita #longevityblackswans



Longevity black swans:

Looking beyond past trends to what potential disruptive developments in medicine, healthcare, technology and lifestyle may mean for life expectancy

Guy Coughlan
Chief Risk Officer, USS
24 April 2018

Paul Kitson
Partner, PwC

This work was carried out in 2017 and first presented at the "Longevity 13" Conference held in Taipei, Taiwan 21 September 2017.

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- **Introduction: What is a longevity Black Swan?**
- Drivers of longevity extension
 - Lifestyle impact
 - Health environment impact
 - Medicine impact
 - The facilitating role of technology
- A realistic disruptive scenario

What is a “black swan”?¹

A Black Swan is ...

an event or occurrence that deviates significantly beyond what is normally expected and that would be extremely difficult to predict

Characteristics:

- A low-probability outlier, beyond experience and expectation
- It has an extreme impact
- It is explainable afterwards, despite being difficult to predict

1. Nassim Nicholas Taleb, "The Black Swan: The Impact of the Highly Improbable."

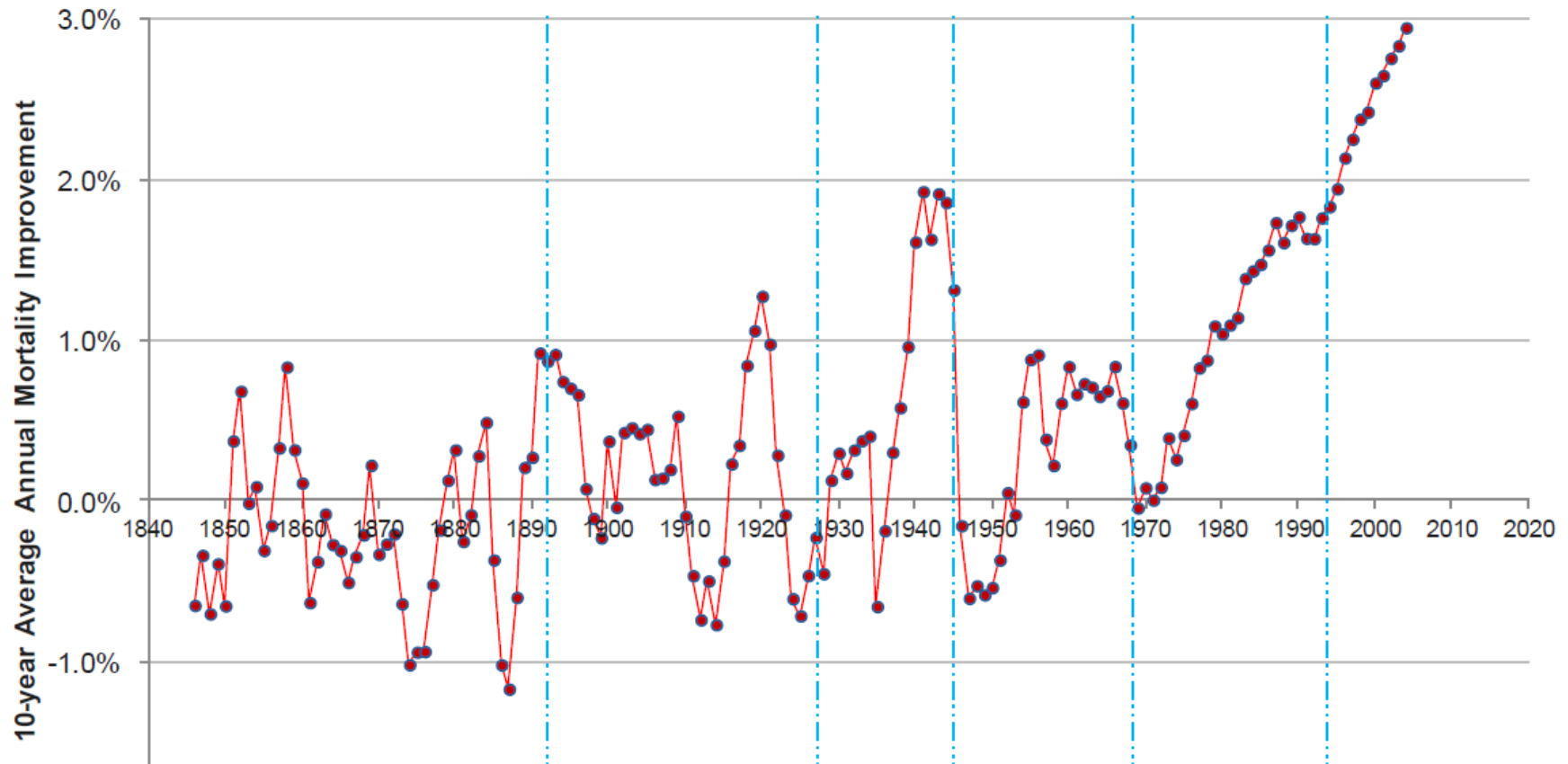
Key question is a question of risk

Is there potential for significant extension of human lifespans?

There are potentially enormous financial, social, political implications

Do past mortality improvements suggest a black swan?

Mortality improvement rates for UK males aged 75-85¹



Source: RMS (2012). "Longevity Risk: Setting the long-term mortality improvement rate. What medical science tells us about future longevity risk"

Is there scope for a future longevity black swan?

Possible black swans include:

- Closure of the LE gap between different socio-economic classes?
- Closure of the LE gap between countries?
- Increases in overall LE driven by advances in lifestyle, health provision and medicine?

Potential drivers likely to include “disruptors” related to:

- Government policy (health, social, economic)
- Education
- Affluence
- Medical science
- Big data
- Technology

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There are three well-established categories for the drivers of gains in life expectancy

Lifestyle	Health Environment	Medicine
<ul style="list-style-type: none">• Diet• Exercise• Smoking• Health-consciousness	<ul style="list-style-type: none">• Healthcare provision• Public health• Social support• Housing & sanitation• Pollution	<ul style="list-style-type: none">• Treatments:<ul style="list-style-type: none">• CVD• Cancer• Respiratory• Dementia• Future developments:<ul style="list-style-type: none">• Regenerative medicine• Anti-ageing

These are the obvious starting point for black-swan hunting

Lifestyle: Diet

Japanese
diet

Japan:
BMJ 2016
Size: 79,594

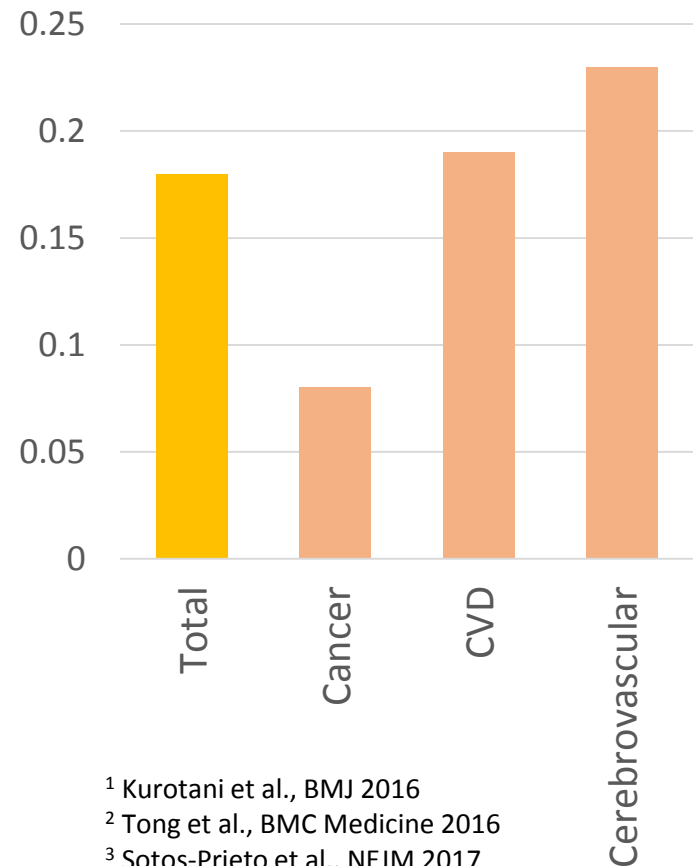
Mediterranean
diet

US:
NEJM, 2017
Size: 73,739

Mediterranean
diet

UK:
BMC Medicine 2016
Size: 23,902

Reduction in mortality hazard rate
for high-quality Japanese diet¹



¹ Kurotani et al., BMJ 2016

² Tong et al., BMC Medicine 2016

³ Sotos-Prieto et al., NEJM 2017

The right diet significantly reduces mortality rates

Lifestyle: Physical exercise

Study of 5823 adults (2017) ¹

- Intense physical exercise
 - Reduces cellular ageing by 9 years
 - Lengthens telomeres
- “High activity” means
 - Jogging 200 minutes per week

Recent 2017 and 2018 studies

- High-Intensity Interval Training HIIT improves decline in muscle mitochondria ²
- Running increases LE by 3 years ³
- Exercise prevents immune system decline ⁴

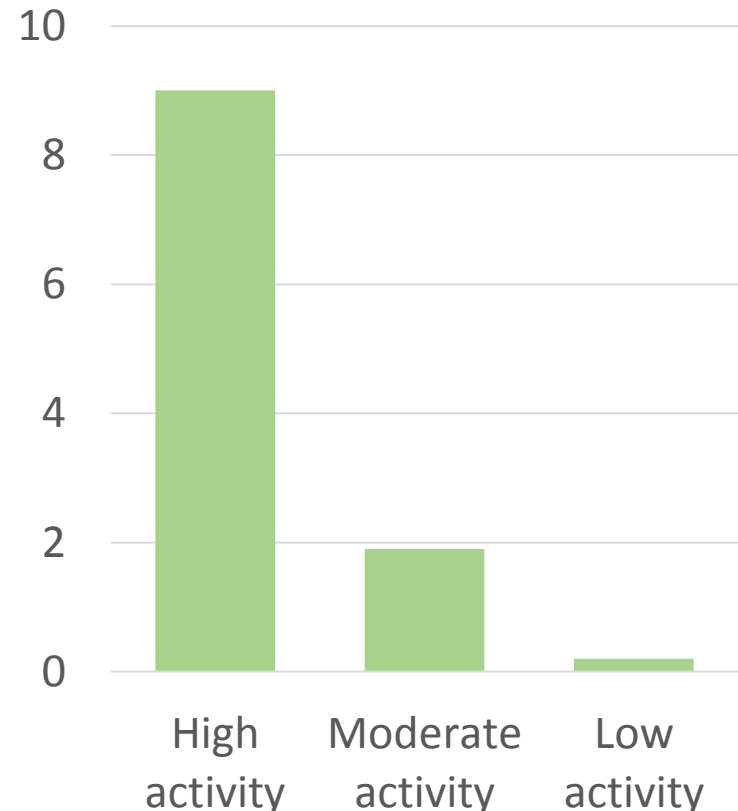
¹ Tucker et al., *Preventative Medicine*, 2017

² Robinson et al., *Cell Metabolism*, 2017

³ Lee et al., *Progress in Cardiovascular Diseases*, 2017

⁴ Duggal et al., *Aging Cell*, 2018; Pollock et al., *Aging Cell*, 2018.

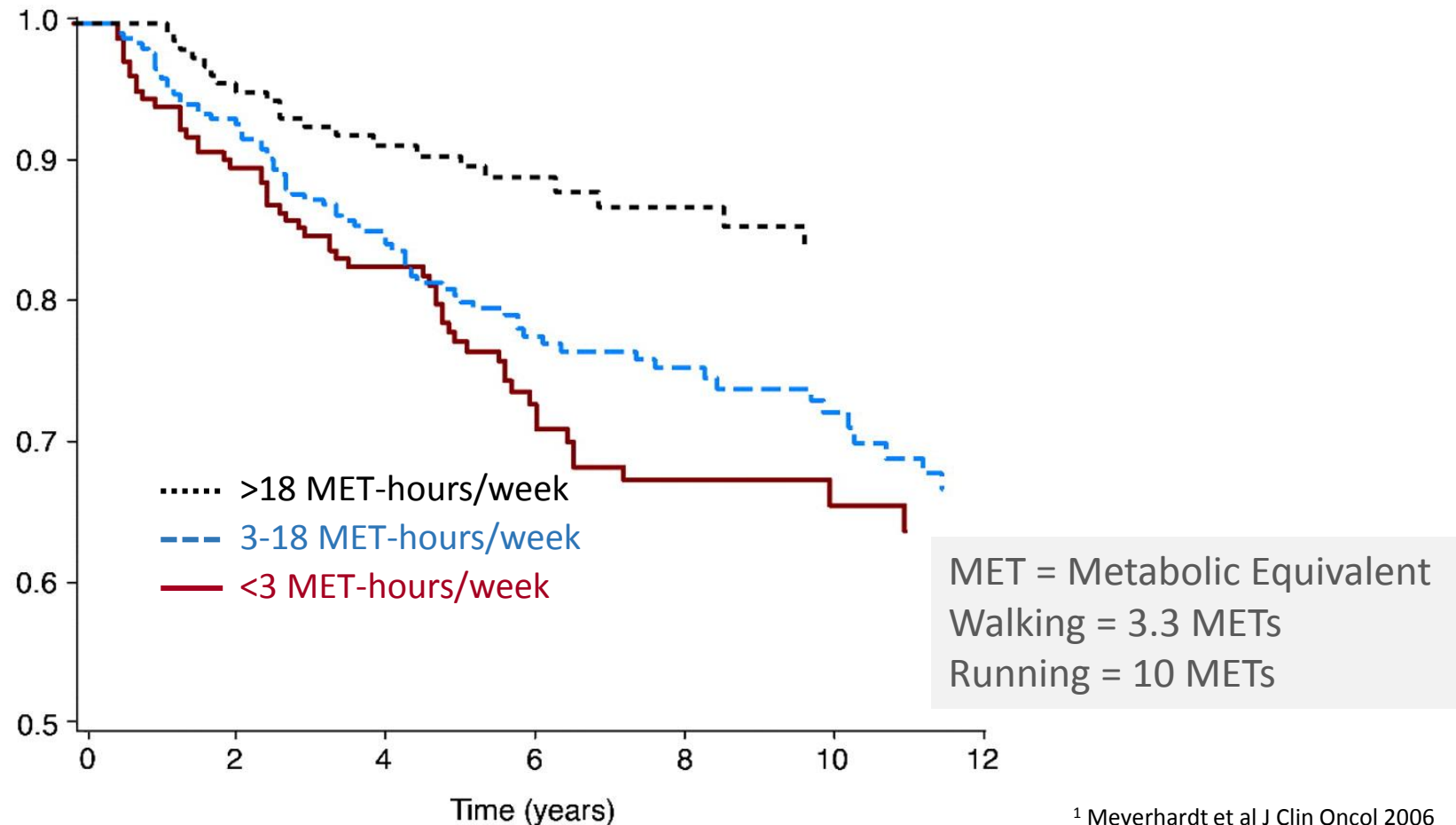
Biological ageing advantage (years) relative to sedentary adults¹



Intense exercise significantly reduces cellular ageing and increases LE

Exercise also boosts cancer survival

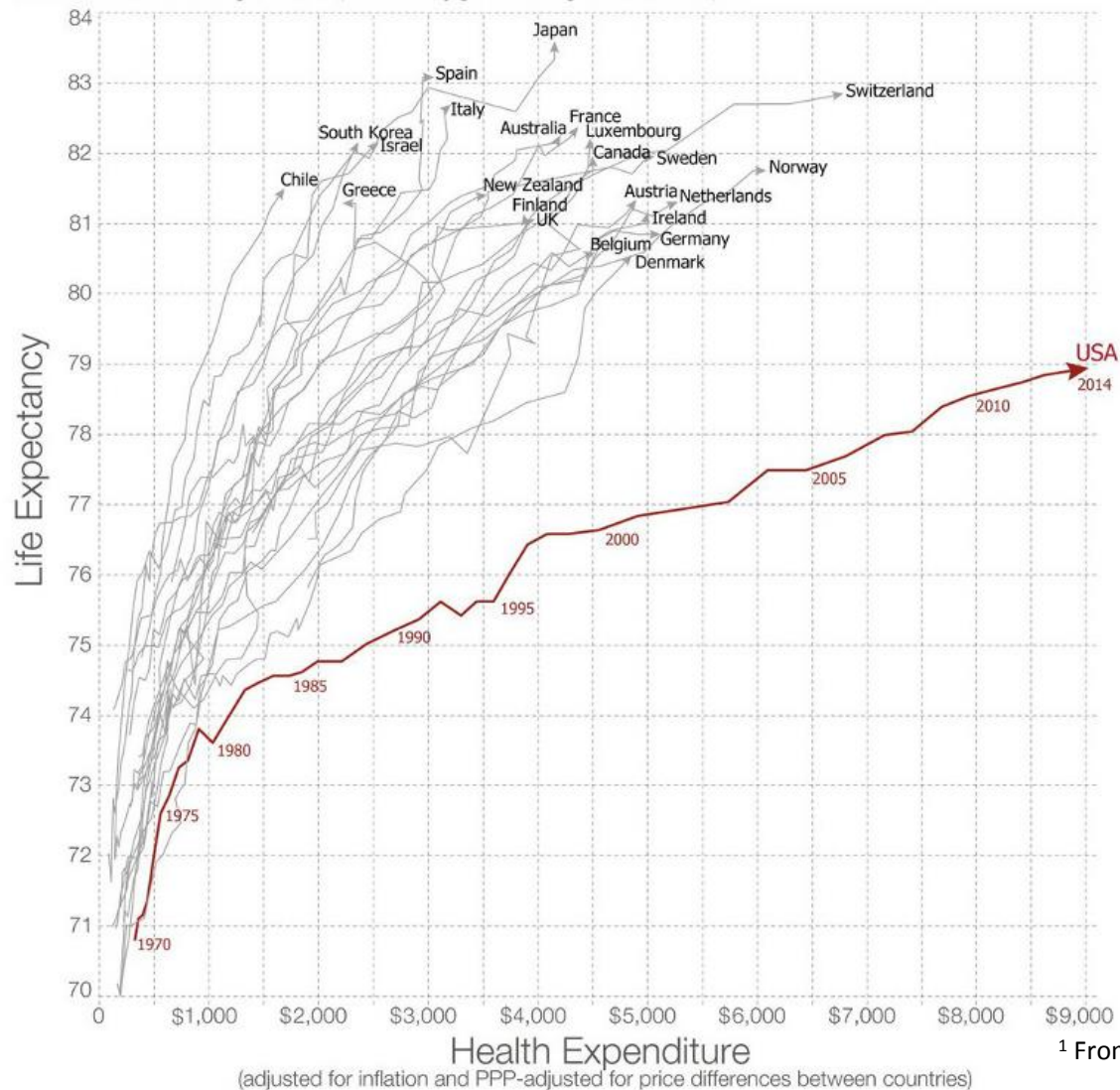
Survival rates colorectal cancer (proportion alive)¹



Again, the more intense the exercise the better

Health environment: LE rises with health expenditure

Life expectancy vs. health expenditure 1970-2014¹



Health environment: Pollution impact

- There is a negative correlation between LE and concentration of PM2.5 (particles <2.5 micrometres diameter)

US study 2009¹

- 217 counties, 51 cities
- Reducing concentration of PM2.5 by 10 micrograms per cubic metre increased LE by 0.77 years

Similar Western studies

- Increase in concentration by this amount reduces LE:
 - Netherlands: 1.1 years
 - Finland: 1.37 years
 - Canada: 0.80 years

EPIC China study 2017²

- 154 cities over 2004-2012
- Difference in LE north vs south of Huai river: 3.1 years
- Due to air pollution from coal burning

¹ Pope et al., NEJM 2009

² Ebenstein et al., PNAS 2017

There are significant LE benefits from clean air

Even regulators are predicting a step-change in the impact of medical science

“New technologies ... hold out the potential to transform medicine and create an inflection point in our ability to treat and even cure many intractable illnesses.”

*FDA Commissioner Scott Gottlieb, M.D.
30 August 2017*

Personalised medicine: Immunotherapy has been generating headlines

FDA U.S. FOOD & DRUG
ADMINISTRATION

30 August 2017

FDA News Release

FDA approval brings first gene therapy to the United States

CAR T-cell therapy approved to treat certain children and young adults with B-cell acute lymphoblastic leukemia

“We’re entering a new frontier in medical innovation with the ability to reprogram a patient’s own cells to attack a deadly cancer.”

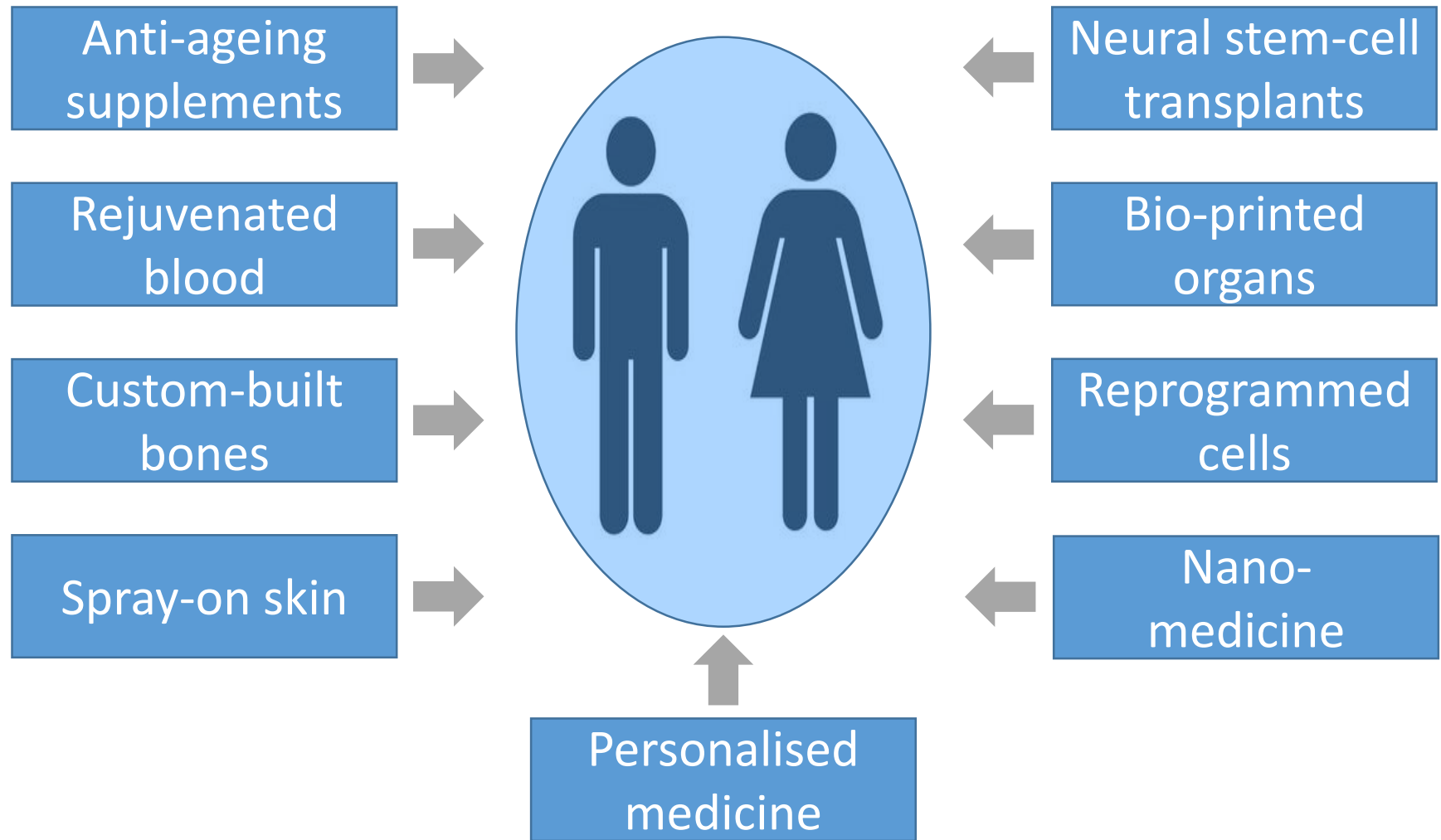
FDA Commissioner Scott Gottlieb, M.D.

Cost: \$475,000



Photo: Novartis

New frontiers: Regenerative medicine and anti-ageing research



Significantly increased life expectancy(?)

Regenerative medicine embraces many approaches

- A multi-disciplinary approach involving methods to regrow, repair or replace damaged/diseased cells, organs or tissues

Tissue engineering

Customised materials (cells and synthetics) to replace injured or diseased tissues

Cell therapy

Getting cells to grow into different kinds of tissue to heal an injury or cure a disease

Artificial organs

Keep patients alive while they await a donor organ, and sometimes eliminate the need for a transplant

Other therapies

Individualised gene therapy, nanomedicine

Tissue engineering has been making steady – but not black-swan-like – progress

Medical  press

Diabetics get blood vessels made from donor cells

June 27, 2011 By MARILYNN MARCHIONE , AP Medical Writer

2011

Medical Daily

Esophagus Grown And Transplanted With Tissue Engineering In Regenerative Medicine Breakthrough

Apr 15, 2014 04:22 PM By John Ericson

2014



RESEARCH & INNOVATION

HORIZON
The EU Research &
Innovation Magazine

Living heart valves grown in laboratories

12 November 2015

2015

Cell therapy is making significant progress

- Induced Pluripotent Stem cells (iPS cells) are 10 years old
 - Stem cells from other cells e.g., ordinary skin cells

Retinal cells

- Treatment for blindness, macular degeneration
- Clinical trials are underway

Blood platelets

- Mass production now possible
- Treatments for cancer, trauma, transplants, surgery
- Clinical trials Japan, US 2018, Europe 2019

Neurons

- Treatment for Parkinson's disease
- Successful animal trials completed with monkeys

Recent breakthrough: Reprogrammed retinal cells transplanted from donor

nature
International weekly journal of science

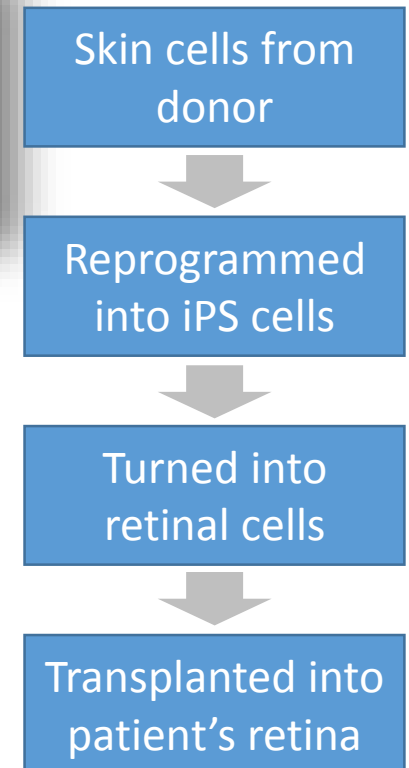
28 March 2017

Japanese man is first to receive 'reprogrammed' stem cells from another person

World-first transplant, used to treat macular degeneration, represents a major step forward in movement to create banks of ready-made stem cells.

→ Treatment to arrest age-related macular degeneration

- In 2014 a Japanese woman underwent similar procedure, but using her own skin cells
- A year later, her vision had not deteriorated further



Recent breakthrough: Production of blood stem cells

nature
International weekly journal of science

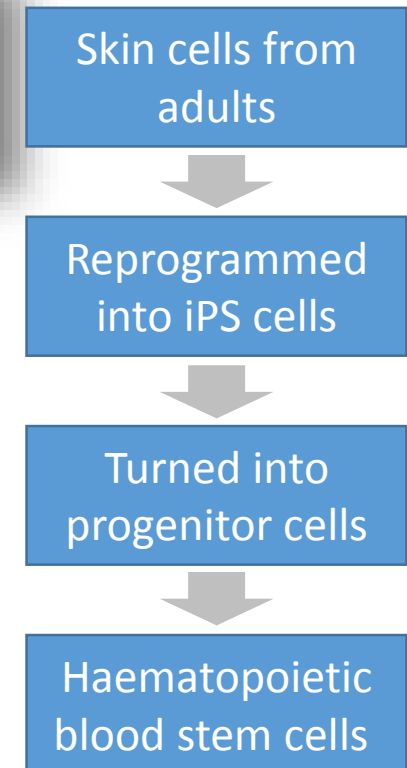
17 May 2017

Lab-grown blood stem cells produced at last

Two research teams cook up recipe to make long-sought cells in mice and people.

→ Treatment leukaemia and other blood disorders

- Mature cells transformed into primordial blood cells that regenerate themselves and the components of blood.



Recent breakthrough: Therapies to reverse age-related cognitive decline



8 August 2017

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

Arc restores juvenile plasticity in adult mouse visual cortex

A single gene “Arc” can rejuvenate the plasticity of the mouse brain.



30 Aug 2017

Reprogrammed cells relieve Parkinson's symptoms in trials

Monkeys implanted with neurons derived from stem cells showed sustained improvement after two years.

Anti-ageing: Many interventions have been highly successful in extending lifespans of lab animals

- Caloric restriction
- “Fasting mimicking diet” (FMD)
- Dietary supplements (drugs)
- Tweaking genes
- Repressing inflammation genes in the brain
- Transfusing blood of the young into the old
- Extension of telomeres
- Senescent cell removal

Recent breakthroughs: Advances in anti-ageing treatments

nature International weekly journal of science

3 Feb 2016

Destroying worn-out cells makes mice live longer

Elegant experiment confirms that targeting senescent cells could treat age-related diseases.

- 25% increase in median life span
- Healthier

TIME | Health

23 Mar 2017

Scientists Can Reverse DNA Aging in Mice

- Repair DNA damage due to age or radiation
- NASA is interested

Can success with animals be translated into humans?

In 2016 400-year-old Greenland Sharks were discovered!

For round worms (*C. elegans*) scientists have achieved a 10-fold increase in lifespan!

- The round worm has only 959 cells
 - Yet over 550 genes have been found to modulate lifespan
- Humans are much, much more complicated

Despite the hype, our best estimate is we still have a long way to go

Very smart, very successful people with huge resources are turning to the challenge of extending life

Exclusive: TIME Talks to Google CEO Larry Page About Its New Venture to Extend Human Life

Bold project, to be led by biotech pioneer Arthur Levinson, will tackle some of health care's biggest problems

By TIME Staff | Sept. 18, 2013

≡ TIME

The Obsession With 'Curing' Aging Is Now Big Business

by Laura Lorenzetti

@lauralorenzetti

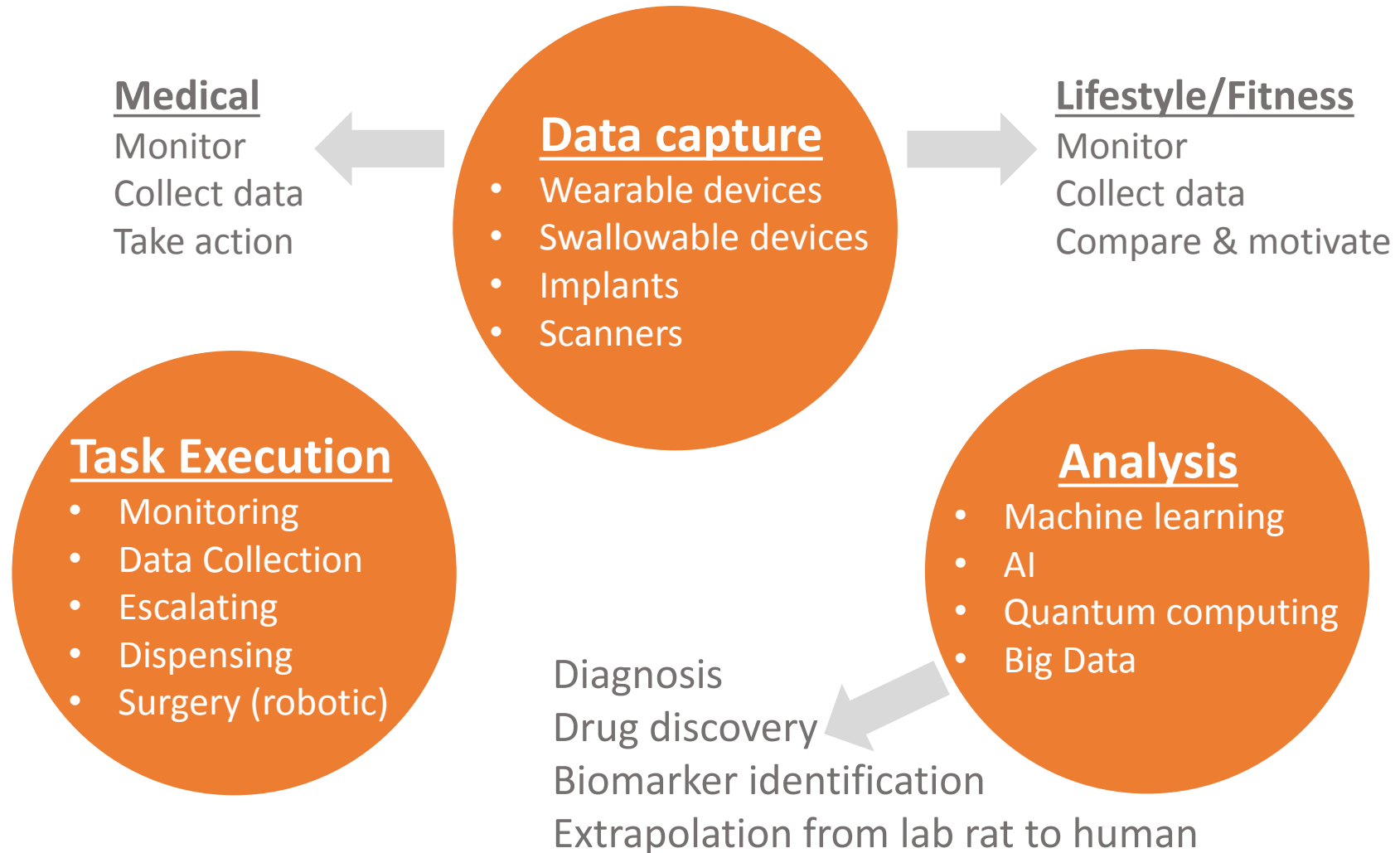
MARCH 7, 2016, 6:00 AM EST

Tech titans bankrolling it.

≡ FORTUNE

1. Peter Thiel – Founder of PayPal
2. Bill Maris – President “Google Ventures”
3. Arthur Levinson – ex-CEO & Chief Scientist Genentech; CEO Google’s “Calico”
4. Dave Gobel – co-founder of the Methuselah Foundation
5. Craig Venter – Key contributor to first human genome decoding
6. Martine Rothblatt – Founder Sirius Satellite Radio; CEO United Therapeutics

The role of technology in increasing life expectancy is multifaceted



Relevant technology is evolving extremely fast and costs plummeting

Let us return to the original question:

Is there potential for significant extension of human lifespans?

- There are many scenarios that could potentially lead to a large extension to human life spans
- Technology is likely to play a central role in all of them
- The scenario we have explored is one possibility, but not the most extreme by a long way

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A range of views exist on the future of longevity change

Exponential Growth?

“What I’m after is not living to 1,000. I’m after letting people avoid death for as long as they want to.”

Aubrey De Grey

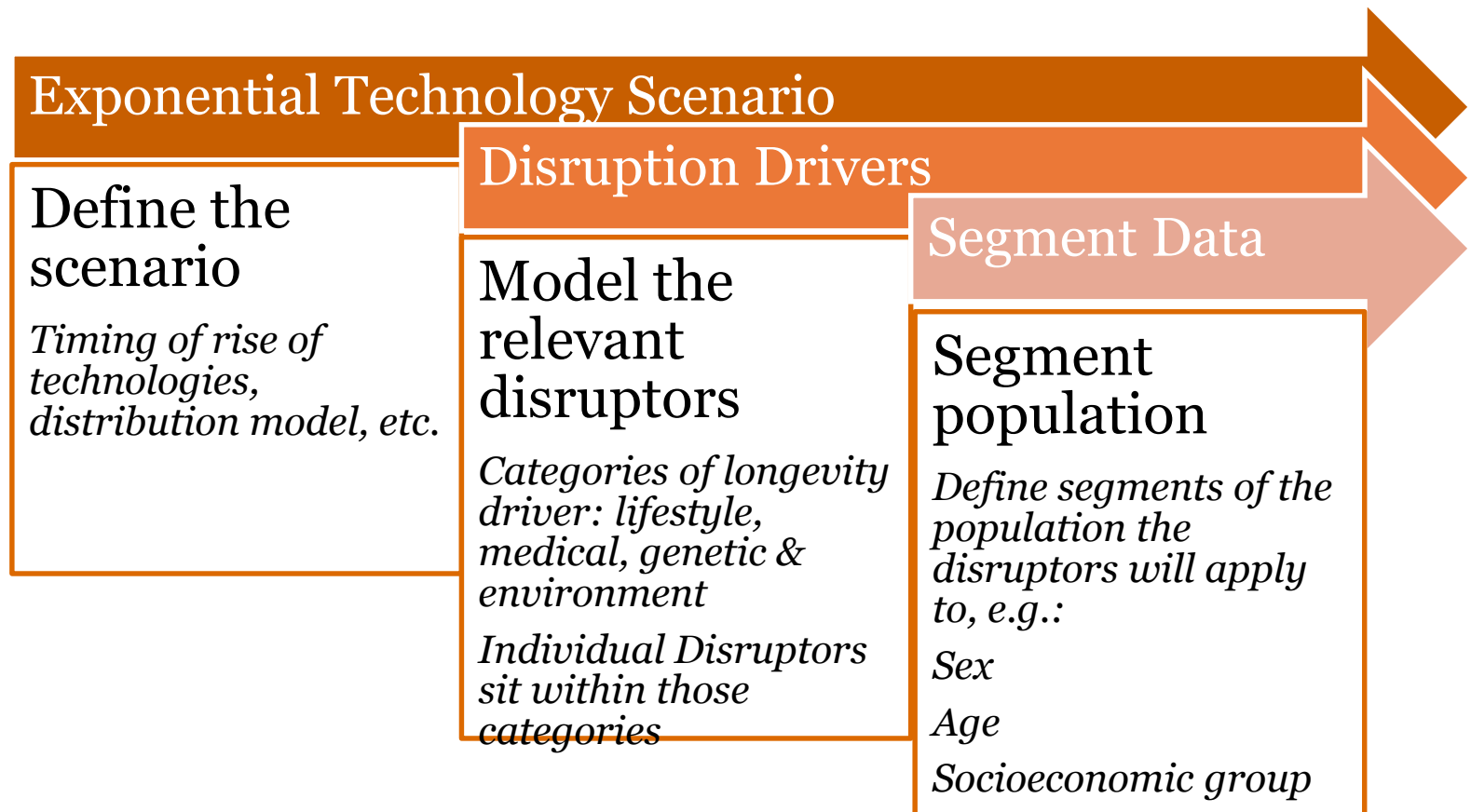


Stagnation?

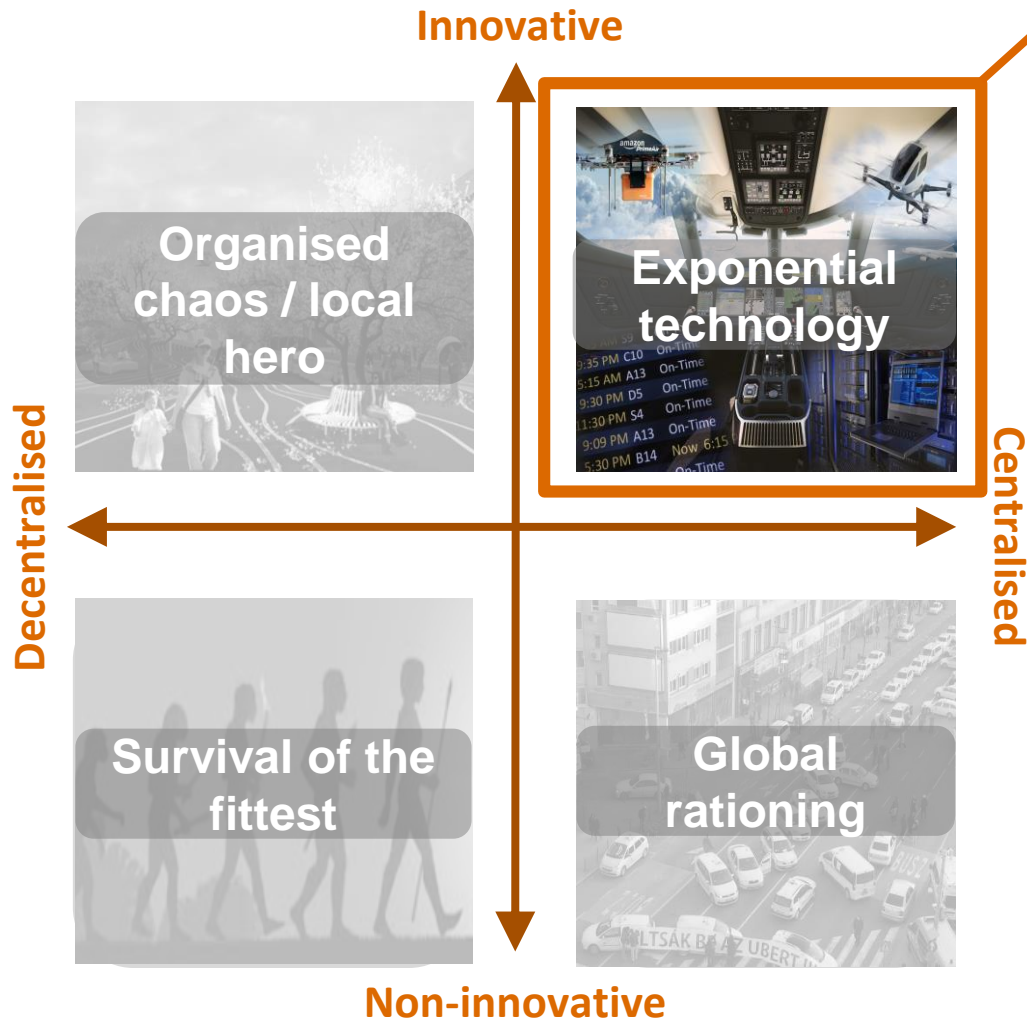
“While eliminating smallpox and curtailing cholera added decades of life to vast populations, cures for the chronic diseases of old age cannot have the same effect on life expectancy. A cure for cancer would be miraculous and welcome, but it would lead to only a three-year increase in life expectancy at birth.”

S. Jay Olshansky

Modelling methodology



Define the scenario (path of disruption)




- **Economic** – across industries machines and automation replace traditional roles to make work more productive and efficient.
- **Technological** – science-led sectors such as artificial intelligence, 3D printing and autonomous vehicles experience exponential growth.
- **Social** – society witnesses increased inequality.
- **Political** – governance takes new forms with control through the state and data.

Define the disruptors

		Magnitude	
Likelihood		Uncertain	Reasonably certain
	Uncertain	<p>Gene editing</p> <p>Understanding of the microbiome</p> <p>GH/IGF1 axis age retardation therapy</p> <p>Telomere extension</p> <p>Nanomedicine</p> <p>Poor access to care</p> <p>Antibiotic resistance</p> <p>Negative mortality effect of widely used drug</p>	<p>Reduction in air pollution in major cities</p> <p>Obesity wipeout</p> <p>Smoking cessation</p> <p>Improved/universal flu vaccination</p> <p>Xenotransplantation</p> <p>Social isolation</p>
	Reasonably certain	<p>Autonomous vehicles reduce accidental deaths</p> <p>Polypill</p> <p>Technology improves access to care</p> <p>Personalised medicine</p> <p>3D Printing replacement organs</p>	<p>90% of vehicles electric</p> <p>Real time medical risk technology</p> <p>Immunotherapy</p> <p>Stem cell therapy</p> <p>Artificial Intelligence in medical intervention</p>

Define the disruptors (an example)

Disruptor and Category

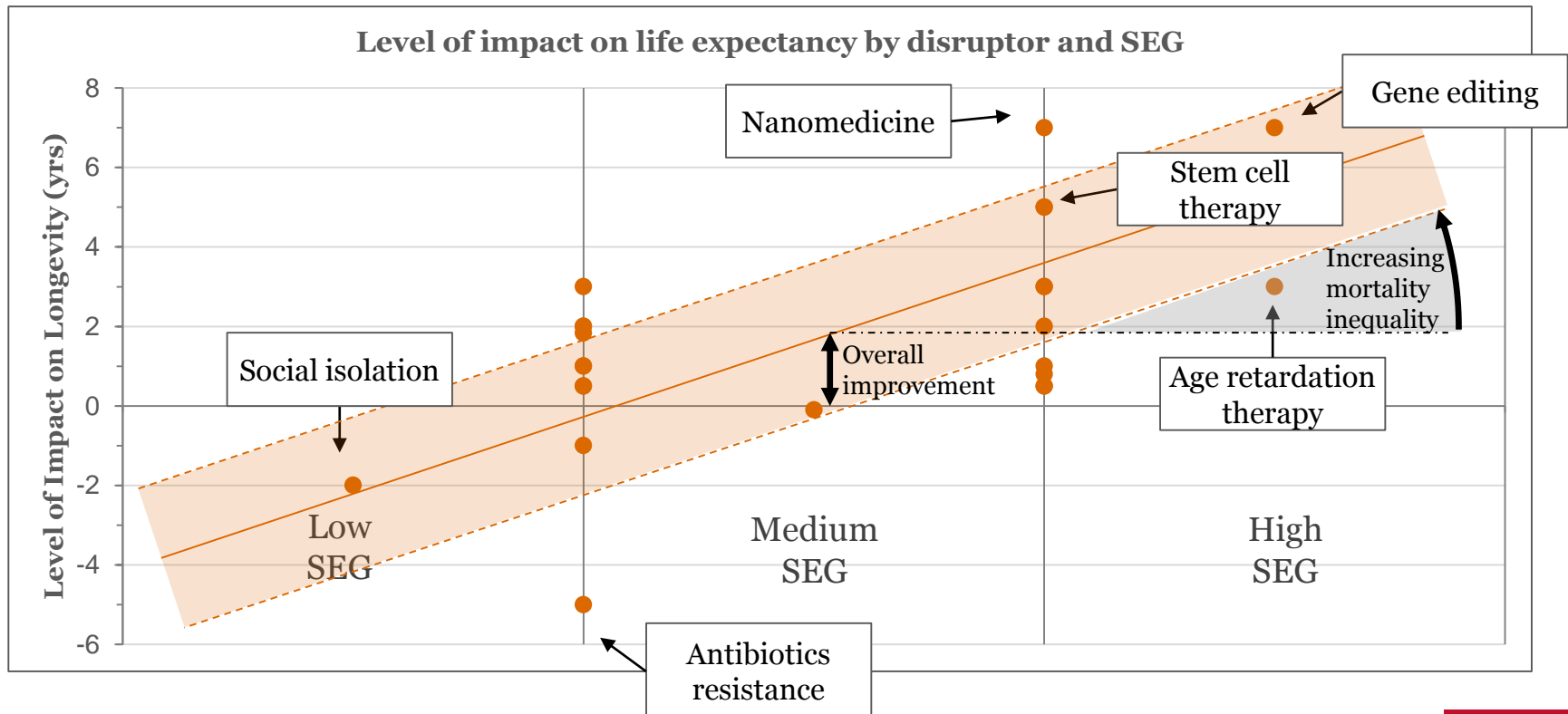


Disruptor No.	Disruptor	Category	Estimated impact on life expectancy (yrs)	Time until start (yrs)	Time taken to end (yrs)
15	Stem cell therapy	Medical	+ 1 < t ≤ 10	5 to ≤ 10	20 to ≤ 40

Quantum of impact and timing



Define the impact by population segment

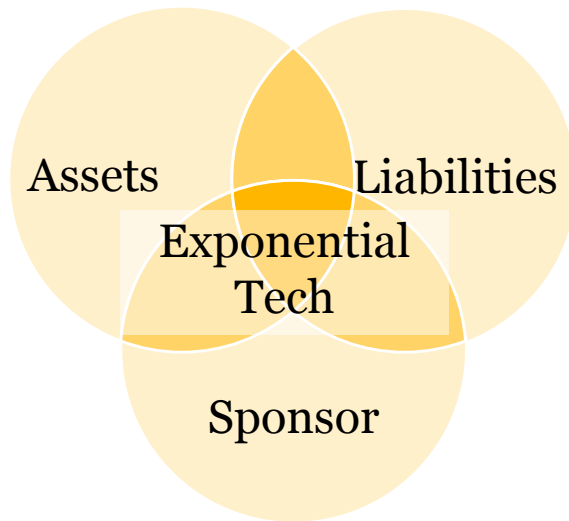


We used output from the RMS LifeRisks model to assist in calibrating the combined impact of the Disruptors



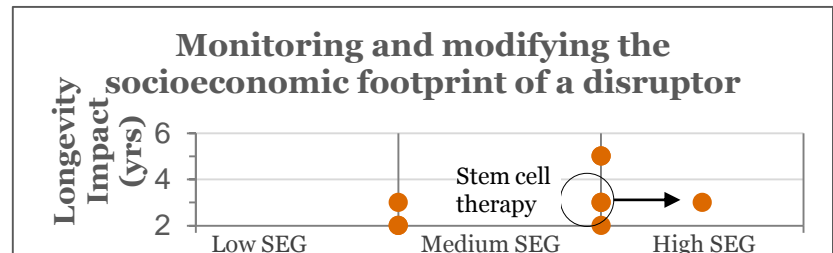
Further work: scheme-wide disruption and monitoring over time

Scheme wide Disruption



Weak signal monitoring

Stem cell therapy	Estimated impact on life expectancy	Time until start (yrs)	Time taken to end (yrs)
Now	+ 1 < t ≤ 10	5 to ≤ 10	20 to ≤ 40
Post liver-transplant breakthrough	+ 1 < t ≤ 10	< 1	20 to ≤ 40



Questions?



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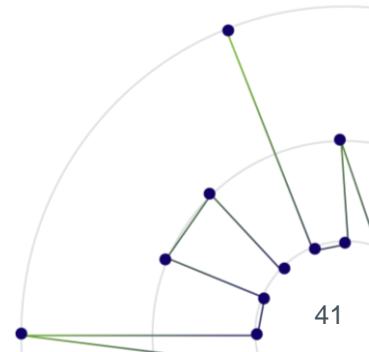
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