



Insurance Collaboration to Save Lives

seek answers, save lives, mitigate loss

The FDA's call for "all hands on deck" for the "catastrophic" decline in U.S. longevity and how proactive insurance leaders can help

12-4-2023



The Insurance Collaboration to Save Lives in one page

is a non-profit led by volunteer insurance leaders

...on mission to save lives and mitigate loss

..with low cost screening, testing, and triage for insureds

...to empower global insurers to save money & lives

Board of Directors

- **Former President** of Progressive
- **Actuary & L/H Regulator** State of Georgia
- **Public Pension Board Chair**, Indiana INPRS
- **EVP & CFO** Specialty & Life Insurance
- **Ins. Attorney**, former ins. AGC
- **Insurance Entrepreneur** & former II #1 equity analyst

Steering Committee

- Actuaries, agents, analysts, data scientists, executives, technologists & underwriters as well as clinicians, researchers, MDs, MPH, RNs, and PhDs

Mortality is elevated

- Working age mortality continues **~20% excess** (age 15-45, CDC 2023)

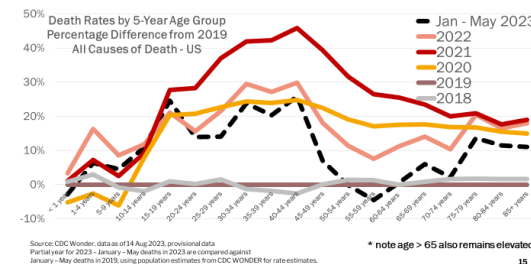
Morbidity is up too

- Disability is **at all-time record levels** in 2023 (BLS, 2023)

Many conditions elevated

- Major rise in **heart, stroke, liver & kidney** deaths (CDC, as of 2022)
- **Similar findings** in ICD diagnoses (INEK, 2022)

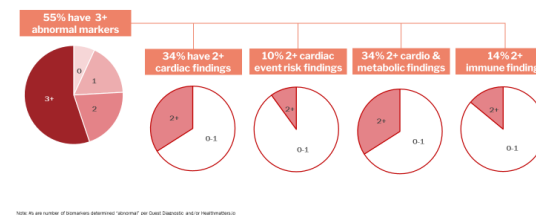
This appears driven by younger age deaths, particularly 15-45*



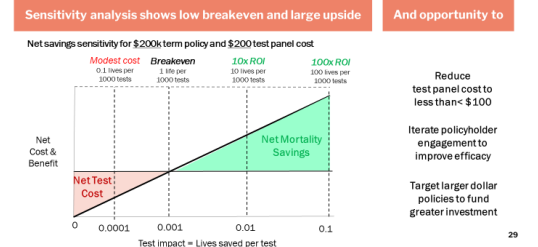
Our advisory team identified five risk profiles for intervention

<p>Signs of possibly serious cardiac concerns</p> <p>14% had 3+ markers of cardiac or circulatory inflammation or injury</p> <p>This includes: hs CRP (inflammation) or dimer (blood clots) tropo (myocardial injury)</p> <p>Pilot data consistent with public data sets - possible widespread blood & cardiac issues</p> <p>Identify and refer for medical diagnosis & care.</p>	<p>Presence of easily addressed cardiac event/risk factor</p> <p>28% had high Homocysteine, a risk-factor for heart attacks</p> <p>Typically caused by vitamin deficiency (B6, B12, folic acid) and genetic factors</p> <p>Homocysteine is toxic and significant contributor to heart attacks/stroke risk.</p> <p>Identify those who need & send them B complex.</p>	<p>Presence of easily addressed immune risk factor</p> <p>24% Vitamin D deficient and 69% were below optimal levels</p> <p>Low levels of Vit. D worsen many immune, heart & other issues.</p> <p>Most in U.S. need daily supplement of Vitamin D, some races, regions, seasons especially.</p> <p>Identify those who need & send them Vitamin D.</p>	<p>Signs of lifestyle diseases & changes needed</p> <p>17% had 3+ markers of heart or kidney disease</p> <p>This includes: TG/HDL, LDL size, A1C, glucose</p> <p>Lifestyle diseases need lifestyle solutions, possibly changes to diet, exercise, fasting, etc.</p> <p>Provide coaching & apps for lifestyle change.</p>	<p>Signs of immune signals which may be COVID related</p> <p>34% elevated monocytes, possibly related to C19</p> <p>28% had very high C19 antibody levels (1.4x to 4.1x median).</p> <p>Abnormally high antibodies may be proxy for acute, long, or other C19 risk, study is needed.</p> <p>If unclear / long COVID symptoms are present, tests may help diagnosis.</p>
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A majority had three or more abnormal markers



Potential returns from proactive risk mitigation are compelling





Disclaimer

The Insurance Collaboration to Save Lives is a non-profit corporation, formed for public benefit to engage and empower global life and disability insurers to take proactive steps screen, test, and triage, to help policyholders improve health, and save lives. This presentation is intended for educational purposes only and does not replace the independent professional judgment of any licensed professional. Statements of fact and opinions are those of the participants and presenters individually and not of any employers, sponsors, partners, or other affiliates or the Insurance Collaboration to Save Lives. The Insurance Collaboration to Save Lives does not assume responsibility for the content, accuracy, or completeness of the information presented. This session may be recorded and published in various media, including print, audio, and video formats without further notice.



I. The FDA's call for "all hands" and how insurers can help.



The FDA has sounded the alarm on “catastrophic” mortality

Dr. Robert M. Califf   ...

@DrCaliff_FDA

We are facing extraordinary headwinds in our public health with a major decline in life expectancy. The major decline in the U.S. is not just a trend. I'd describe it as catastrophic.

1:52 PM · Nov 30, 2023 · **20.6K** Views

 40  49  107  11 

Dr. Robert M. Califf is the Commissioner of the U.S. Food and Drug Administration



The FDA called for “all hands on deck” to address mortality



Dr. Robert M. Califf ✓ FDA

@DrCaliff_FDA

I believe that we need to seriously examine our level of accountability and changes that we can make to help what needs to be an “all hands on deck” effort to continue and amplify the improvement in life expectancy discussed in CDCs latest report.

1:52 PM · Nov 30, 2023 · **611** Views

Dr. Robert M. Califf is the Commissioner of the U.S. Food and Drug Administration



The FDA is asking for help from industry and the public...



Dr. Robert M. Califf ✓ FDA

@DrCaliff_FDA

The government, industry, and the public all have a role to play in improving life expectancy. Let's get to it.

1:52 PM · Nov 30, 2023 · **934** Views

Dr. Robert M. Califf is the Commissioner of the U.S. Food and Drug Administration



So what are the “catastrophic trends” the FDA is seeing?



Today U.S. mortality remains elevated, even post COVID

US Mortality Mortality Monitoring for the United States of America

DEATHS | **MORTALITY** | EXCESS MORTALITY | MAPS | MORE

Percentage | Z-Score | Cumulative | Yearly (% , Cumulative) | Pandemic (% , Cumulative) | Pandemic Ranking (% , Cumulative)

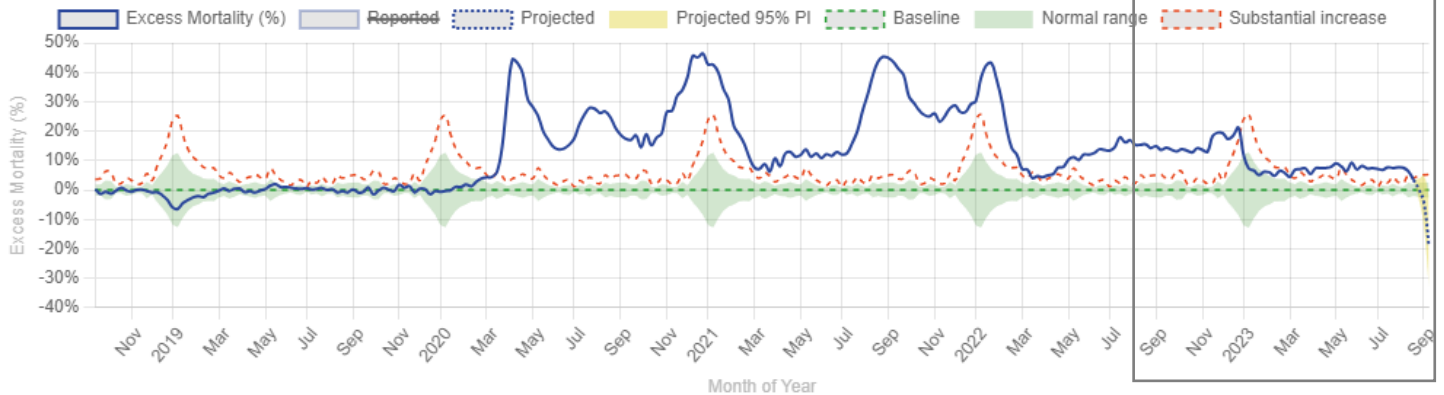
Weekly All-Cause Excess Mortality (Percentage)

These charts shows the weekly percentage excess mortality (age-adjusted, US Std. Pop.) for the United States and its states over time.

Aug 2023
excess = 7.6%

Excess Mortality [United States]

Weekly, All Causes, Age-Adjusted (US Standard Population 2000)

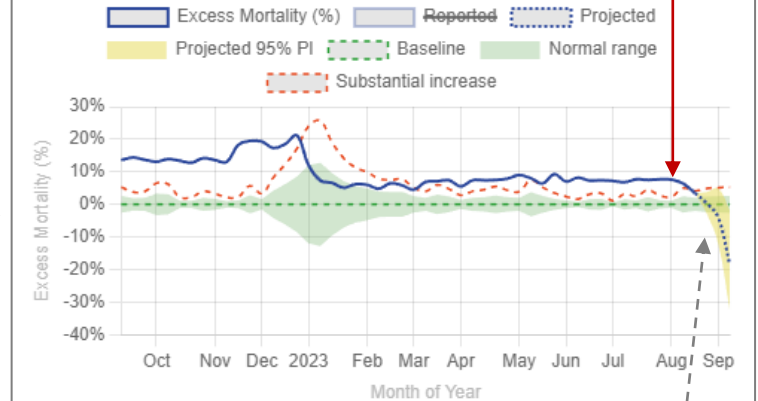


Sources: CDC.gov, Census.gov

Show Months | CSV | JSON | ▲

Excess Mortality [United States]

Weekly, All Causes, Age-Adjusted (US Standard Population 2000)



Sources: CDC.gov, Census.gov

reporting lag

Source:
U.S. Mortality.com, visited 11/6/2023, <https://www.usmortality.com/excess-mortality/percentage>



As always at time of crisis...



Insurance Collaboration to Save Lives

seek answers, save lives, mitigate loss

...insurers are here to help.



What is the Insurance Collaboration to Save Lives?



Insurance leaders saw elevated mortality and came together

life annuity specialist

As Covid Rules Are Relaxed, : Insurers Face 'Trillion-Dollar Question'

Everyone wants to move past Covid. But here are some worrying numbers that life insurers should be paying attention to.



Stirling convenes group to address excess mortality, seeks industry partners

For links to these and others, please see:
<https://www.insurancecollaborationtosavelives.org/media>



Leaders of the Insurance Collaboration to Save Lives

Directors & Officers



Richard H. Watts, Board member at Farmers Group, Inc., Apaly Health and Roost, advisor to numerous PE & VC backed ventures, and former President of Direct Group at Progressive Insurance.



Michael Grasher, EVP & CFO at The Fortegra Group, specialty multi-line insurer, former CFO at publicly traded work comp company, previously a Managing Director and multi-line insurance analyst at Piper Jaffray.



Bret Swanson, Chairman of the Indiana Public Retirement System (INPRS), President of Entropy Economics, LLC, and non-resident senior fellow at the American Enterprise Institute.



Teresa R. Winer, F.S.A., M.A.A.A. L&H Actuary for the State of Georgia's Commissioner of Insurance, member of AAA's NGE Working Group, former VP & two-term SOA board member and GSU RMF board



Noelle H. Sproul, Esq. ICSL Corp Secretary, investment lawyer, former Managing Director in the legal department of a large insurance company, and previously, an attorney at Moore & Van Allen.



Josh Stirling, Founder of the Insurance Collaboration to Save Lives, insurance director, advisor and entrepreneur, former chief insurance & partnerships officer, managing director, and *Institutional Investor* #1 ranked Wall Street analyst

Team Leaders

Medical & Product

- [Steve Cyboran](#), ASA, FCA
- [Edward Loniewski](#), DO, FACOS, FAOAO
- [Tom Lewis](#), Ph.D.
- [Kate Hendricks](#), M.D. M.P.H.
- [Steven Dunlap](#), MD

Analytics & Research

- [Mary Pat Campbell](#), FSA
- [Valerie Chezem](#), ASA
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- [JR Reyling](#), MBA, E.E.
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Marketing & Comm

- [Marci Sheeran](#), CLTC, LUTCF
- [Mitch Bagley](#), agent
- [Rebecca Richey](#), agent
- [Bryan Barber](#), technology

International

- [Adam Chambers](#), Esq.



...formed a non-profit and studied excess mortality & morbidity

IN INSURANCE NEWSNET Your Industry. One source.™

Top Stories

Last 6 months | @insurancenewsnet

Insurance industry coalition forms non-profit to study baffling excess mortality



BEST'S NEWS & RESEARCH SERVICE

LIFE INSURANCE

Insurance Execs Form Nonprofit, Seek to Provide Life Insurers With Tests for Policyholders

For links to these and others, please see:
<https://www.insurancecollaborationtosavelives.org/media>



Developed a new approach to mitigate mortality & morbidity

ThinkAdvisor

How Insurers Can Help Prevent Unexpected Deaths

Unexpected deaths have been rising since the pandemic and could lead to a cascade of costs.



Chief Executive

Screen, Test, Triage: How Life Insurers Can Help Reduce Excess Mortality

This solution is within the industry's grasp and requires no new technology –only CEO leadership to deploy it.



A simple proposal : insurance-led proactive health screening

Proactive
insurers that...

Screen, test
& triage

In-force
policyholders

can mitigate excess mortality & elevated morbidity



An ounce of prevention is tautological in every field...

Health

Save lives and
save money.

**Do well by
doing good.**

Actuarial

Use proactive
screening to identify
insureds to offer health
intervention.

**Use data to reduce
cost & drive ROI**

Technology

TL:DR =
Risk Mitigation
> Risk Transfer

**Move fast &
[save lives]**



Momentum is building for the Insurance Collaboration's effort

December 2023



Greater Health Screenings Could Save Life Insurers Money and Improve Mortality, Group Says

A nonprofit formed by industry executives is proposing insurers test policyholders for a battery of common causes of morbidity.

November 2023

life annuity specialist

More Young People Are Dying, Higher Mortality is in the Forecast

The fix may be greater investments in wellness programs, according to experts.

October 2023

Newsweek

Why Are Death and Disability Rising Among Young Americans? | Opinion

October 2023



'Excess mortality' continuing surge causes concerns

For links to these and others, please see:
<https://www.insurancecollaborationtosavelives.org/media>



Where does the Insurance Collaboration go from here?

Recruiting
global insurers
to pilot these
initiatives

Recruiting
tech & health
partners to build
solutions

Recruiting policy &
regulatory partners
to accelerate this
effort

**Insurers can play a leadership role in this catastrophe
But to save a million lives, we need your firm to help**



II. What's going on, and how did we get here?

“Excess Mortality: a Peek Under The Iceberg”

Presentation to the Society of Actuaries, Society of Insurance Research, and Bermuda International Long Term Insurance & Reinsurance Meetings Aug & Sept 2023



The executive summary : there are just three things to know

1

Younger adult mortality in U.S. is ~20% excess, in 2023 *

2

Morbidity analysis shows wide range of underlying conditions

3

Insurers who take steps to mitigate, can save money and will save lives

***and reported disability rate – a leading indicator of future mortality – is at all-time highs**



A team of volunteers worked for months to answer this

Life
SOA MEETING

Valerie Chezem ASA,MAAA

Valerie Chezem ASA,MAAA
Steven F. Cyboran, ASA, FCA, MAAA, CEBS
Josh Stirling, MBA, A.Re

Excess Mortality

A Peek Under the Iceberg

Session 10C: August 23, 2023

Valerie Chezem, ASA, MAAA, Assistant Actuary, Everence

Josh Stirling, Founder of Insurance Collaboration to Save Lives, Insurtech Advisor, Board Director and Former #1 Ranked Insurance Analyst

Steve Cyboran, ASA, MAAA, FCA, CEBS, CEO, Consulting Actuary, Humaculture, Inc.

Dr. Thomas Lewis, PhD, CEO, Revival Health

Mary Pat Campbell, FSA, MAAA, Vice President, Insurance Research, Conning

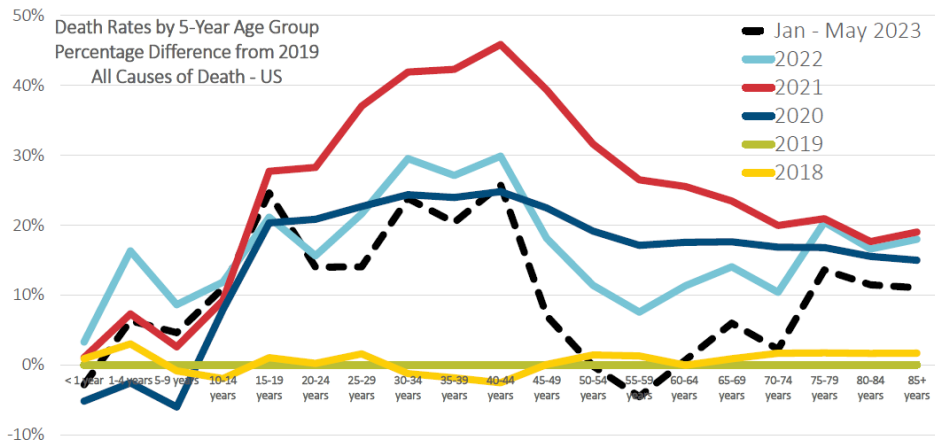
Kate Hendricks, MD, MPH&TM, Former Federal Public Health Official, CDC

Teresa Winer, FSA, MAAA, Actuary, Office of Insurance and Fire Safety Commissioner, Georgia

JR. Reyling, PE, IMBA, Data Scientist, Reyling Analytics

SIR SOCIETY OF INSURANCE RESEARCH

SIR 2023 ANNUAL CONFERENCE



Source: CDC WONDER, data as of 14 Aug 2023, provisional data
Partial year for 2023 - January - May deaths in 2023 are compared against January - May deaths in 2019, using population estimates from CDC WONDER for rate estimates.

Note: see our full team on page 4

Use this QR code to the full 66-page deck by email right now



also available at:

<https://www.insurancecollaborationtosavelives.org/contact>



1

Mortality and morbidity challenges continue even post-COVID

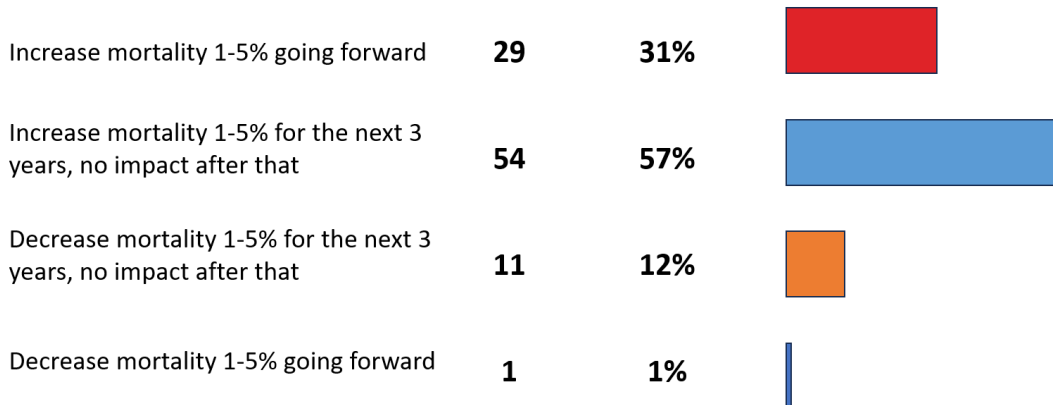


What is happening? Polls at the Society of Actuaries Life Meeting

Actuaries polled in Aug'22
88% think excess mortality continues to 2025+

2022 SOA Life Meeting Poll:

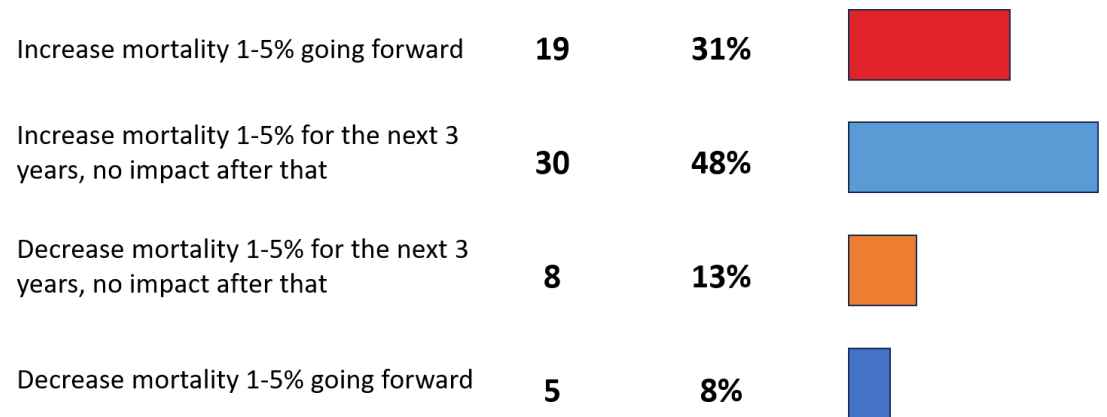
What is the most likely long-term impact of COVID-19 On Group Life mortality in late 2022, into early 2023, and beyond?



Actuaries polled in Aug'23
79% think excess mortality continues to 2026+

2023 SOA Live Life Meeting Result:

Compared to 2019, what is the most likely long-term impact of the pandemic on the age-adjusted all-cause mortality rate in the US, in 2024 and beyond?

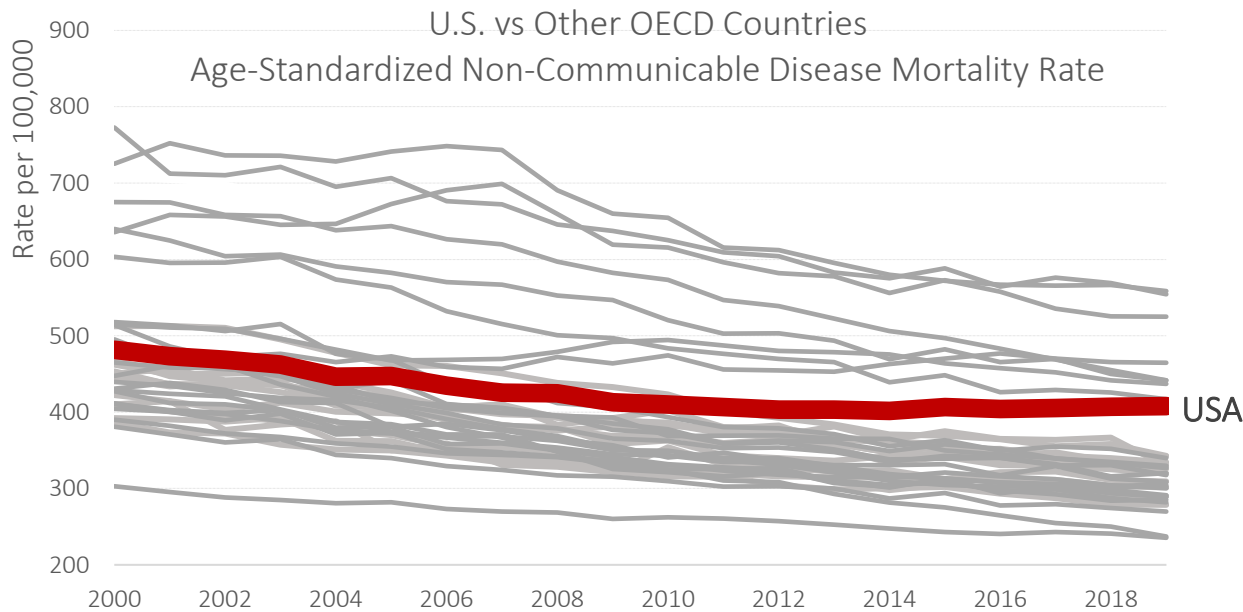


Source: Society of Actuaries polling of meeting attendees at Life Meetings in 2022 and 2023, analysis by ISCL



This is because U.S. has long faced health challenges

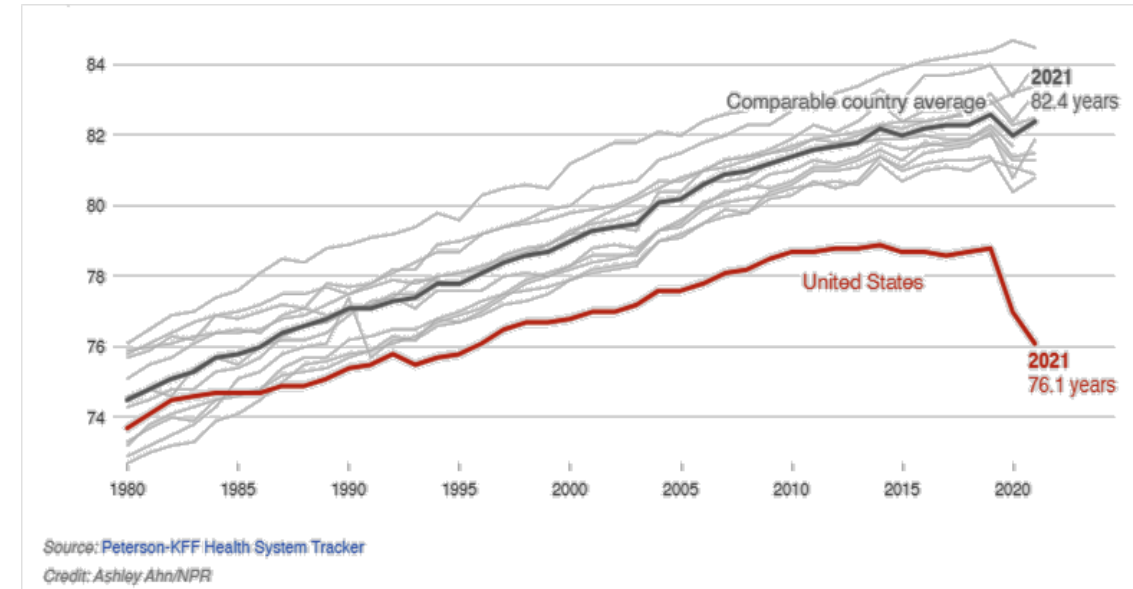
While peers' health improved, U.S. mortality was worsening pre-C19



Source: WHO Global Health Estimates, accessed 15 August 2023, <https://www.who.int/data/gho/data/indicators/indicator-details/GHO/gho-ghe-ncd-mortality-rate>
Excludes communicable diseases like the flu and external causes of death such as homicide and car accidents.

During the pandemic U.S. mortality was worse than peers

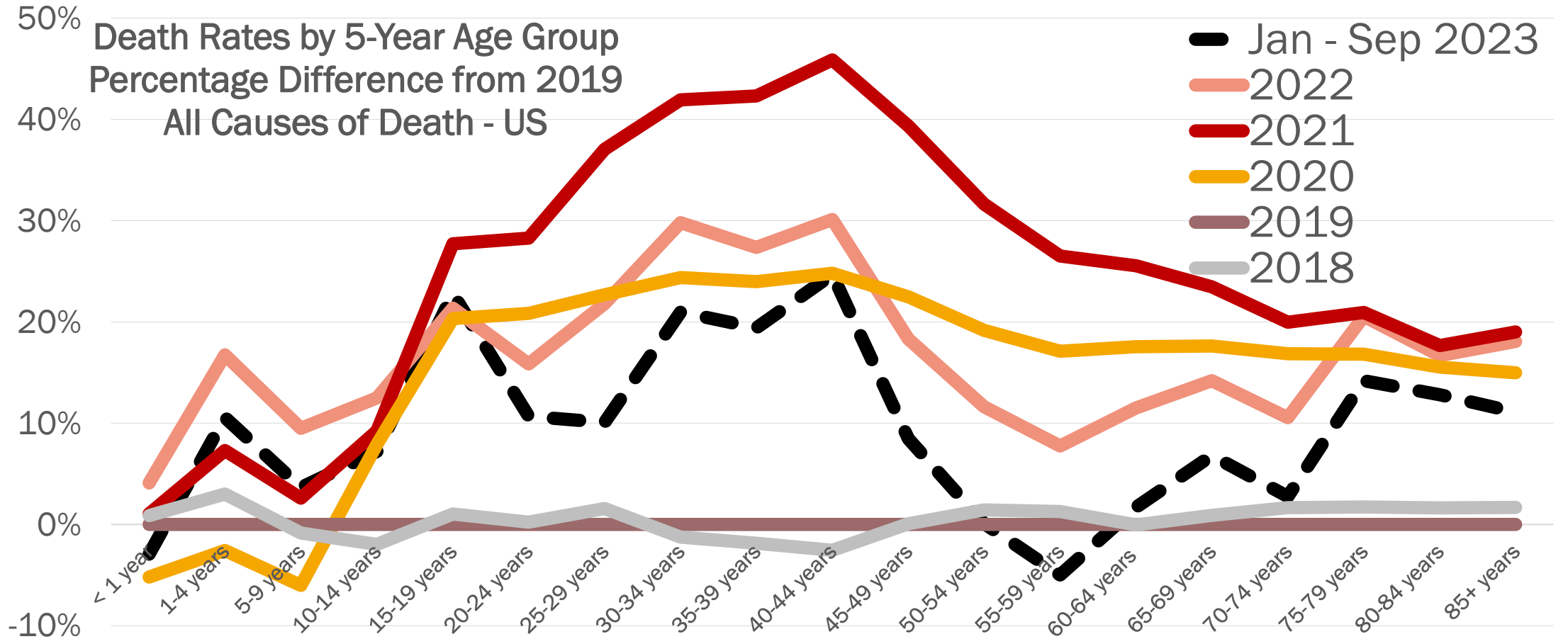
Period Life Expectancy, U.S. vs. Comparable Countries



Source: <https://www.npr.org/sections/health-shots/2023/03/25/1164819944/live-free-and-die-the-sad-state-of-u-s-life-expectancy>



This appears driven by younger age deaths, particularly 15-45*

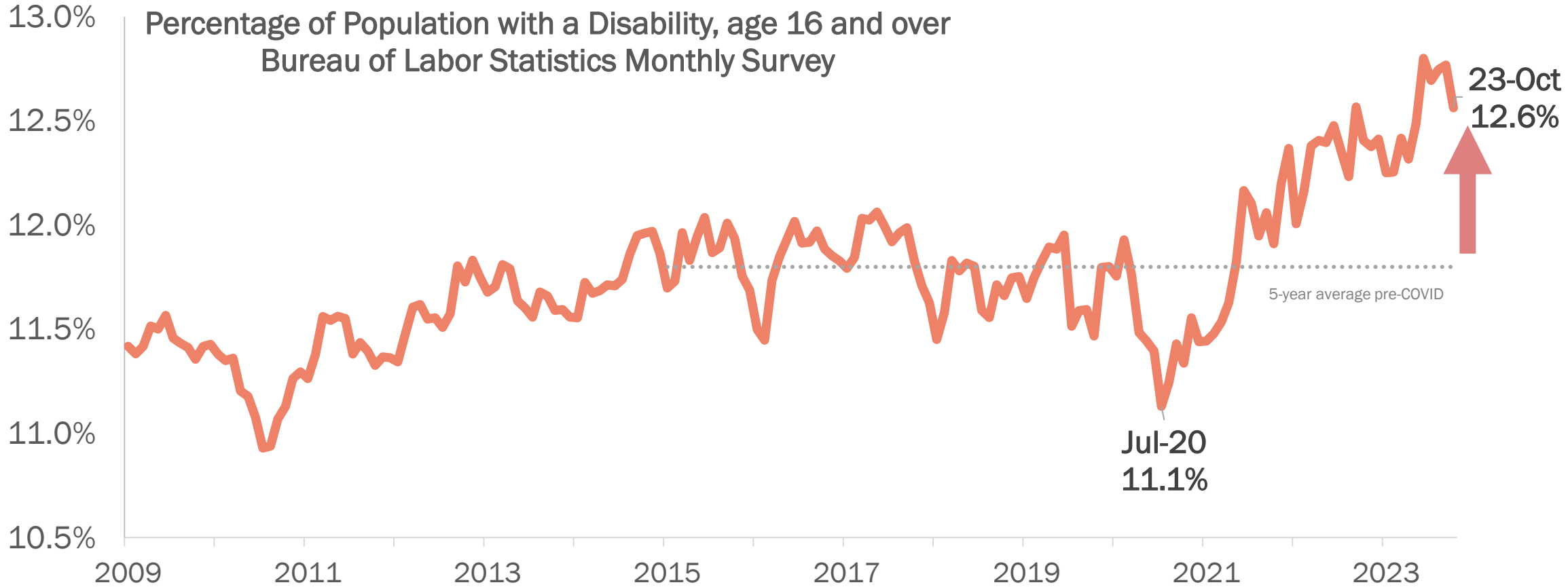


Source: CDC Wonder, data as of 3 Dec 2023, provisional data
Partial year for 2023 – January – September deaths in 2023 are compared against
January – September deaths in 2019, using population estimates from CDC WONDER for rate estimates.

* note age > 75 also remains elevated in 2023



Morbidity trends are also tragic, with disability at record levels



Source: Bureau of Labor Statistics, via St. Louis fed FRED <https://fred.stlouisfed.org/graph/?id=LNU00074597> and <https://fred.stlouisfed.org/graph/?id=CNP160V>, as of 10/1/2023



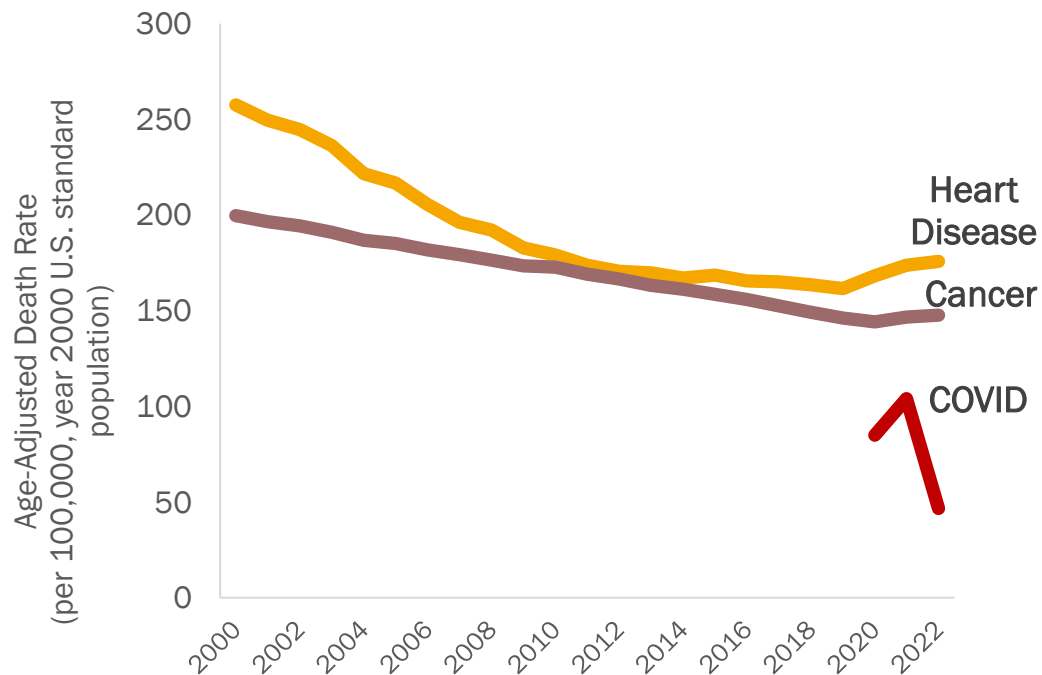
2

Analysis shows many causes, an “iceberg” of health challenges

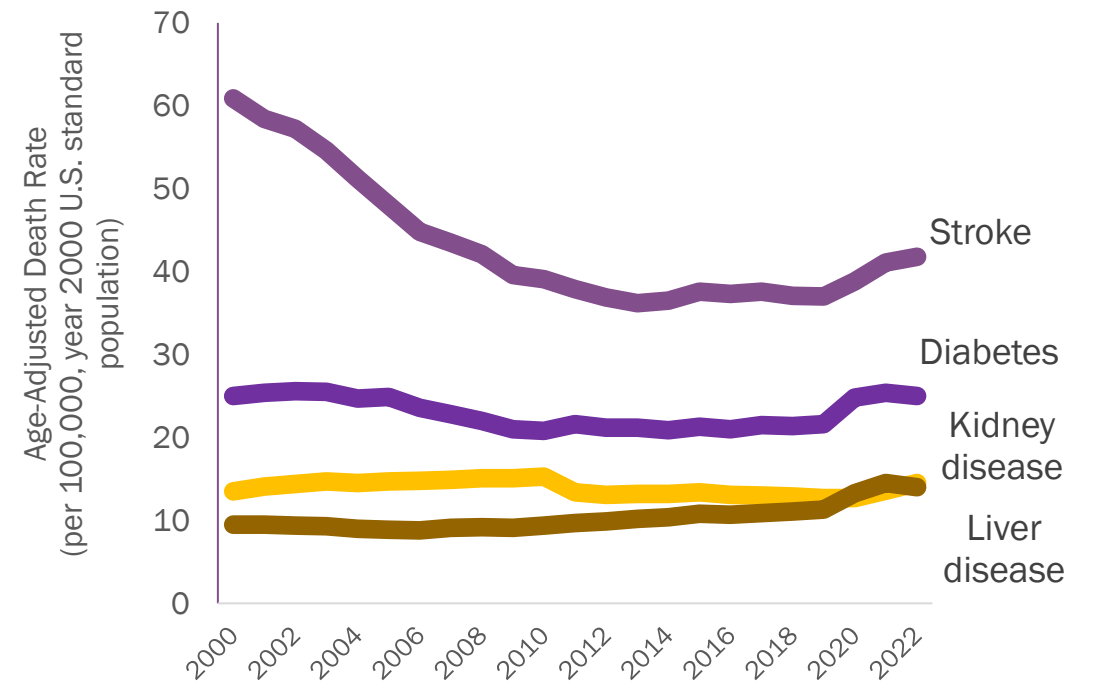


Analysis of U.S. deaths suggests emerging shift in pathology

As COVID declined in 2022...

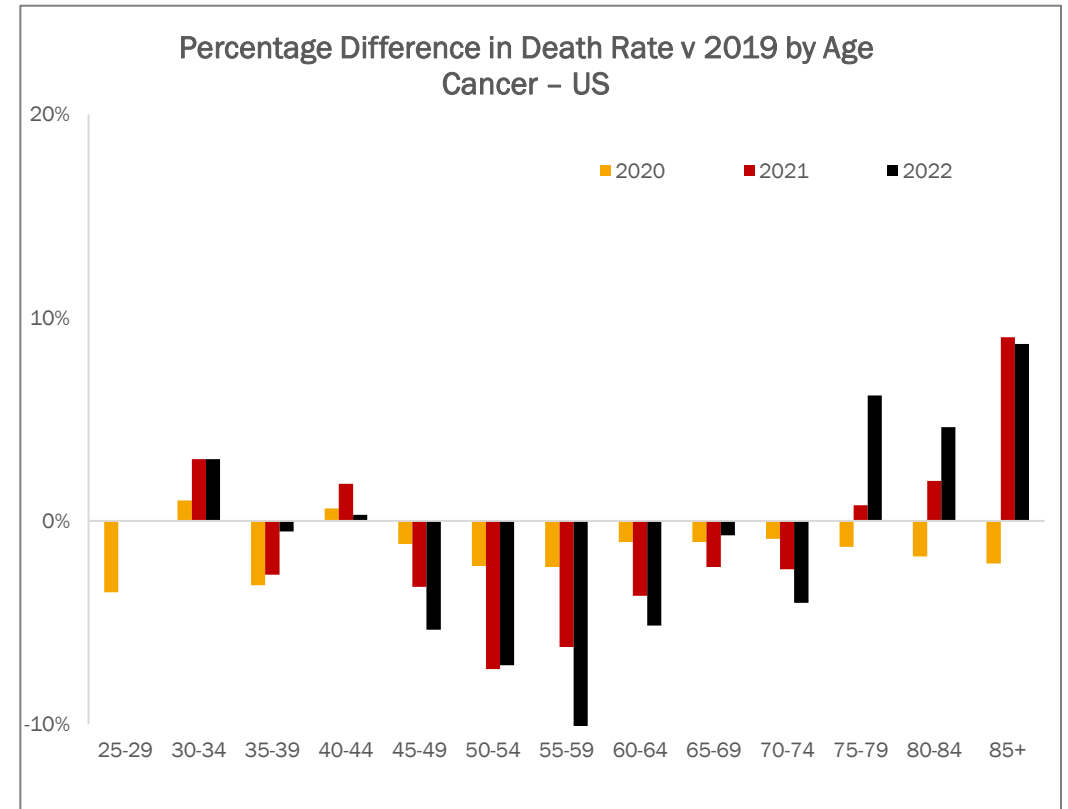
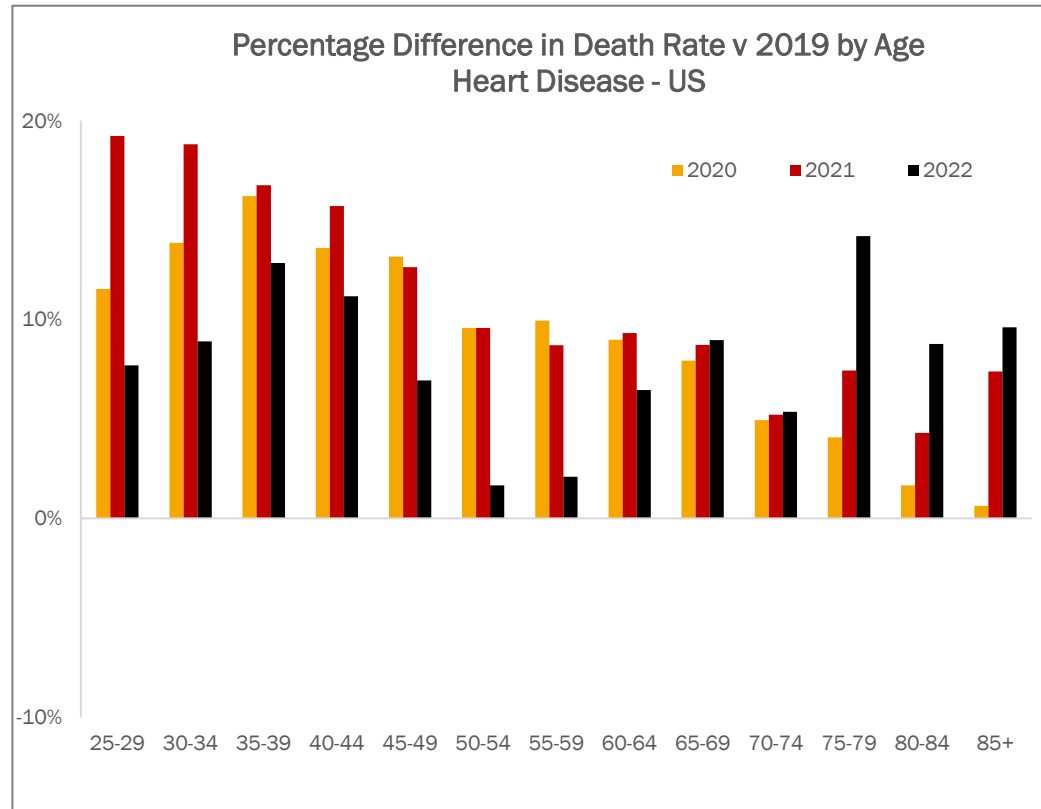


...Other causes rose, including many that are blood related





Cause of death data shows increased cardiac mortality at all ages

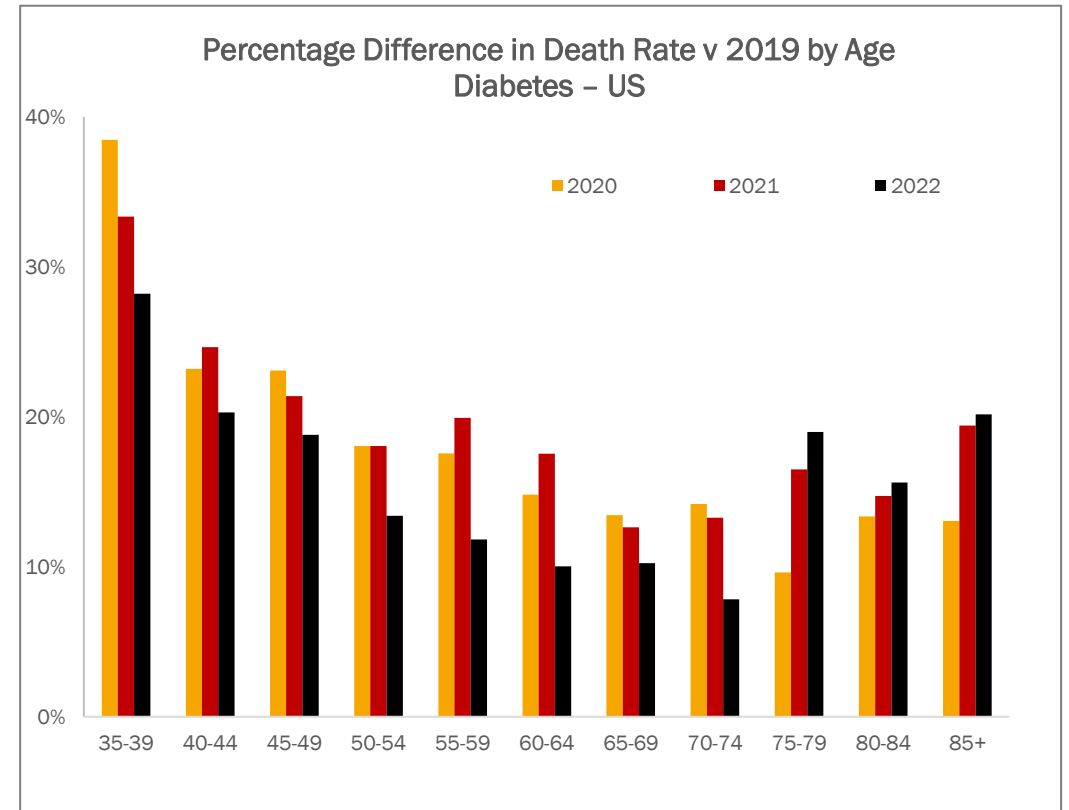
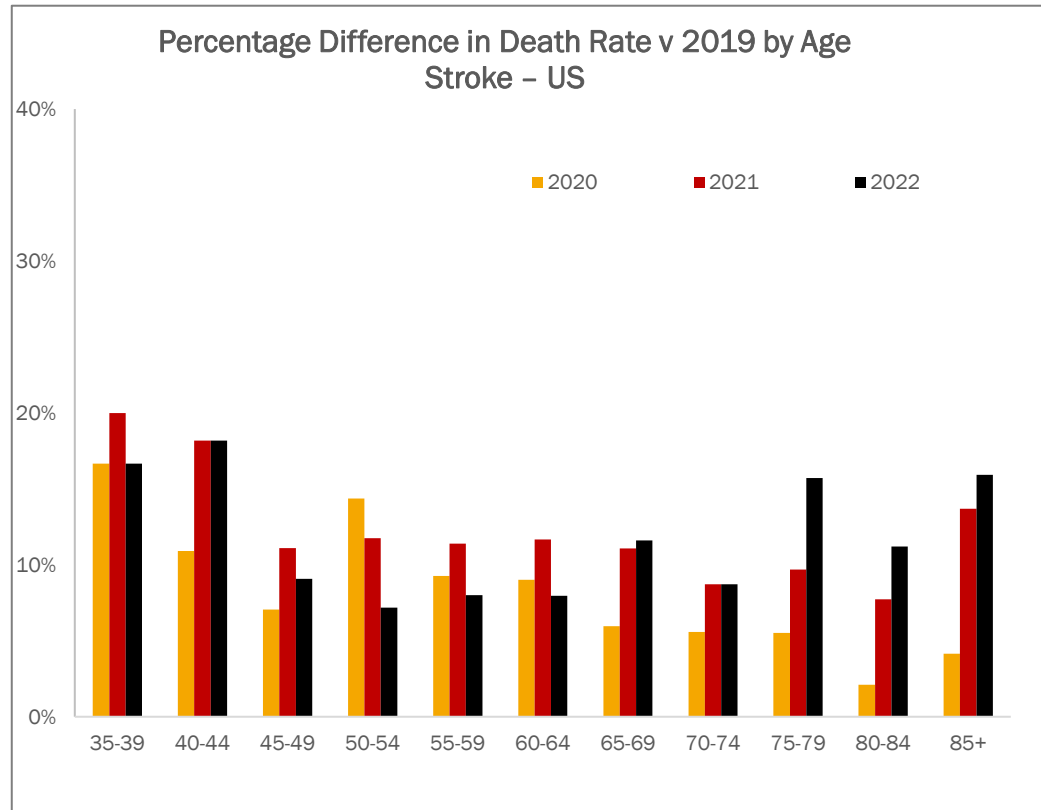


Source: CDC Wonder, data as of 3 Dec 2023, provisional data, primary cause of death. Note small numbers of deaths and/or data not available or not meaningful at younger ages.



Similar – but greater – rise in other notable pathologies (1/2)

Note change in scale from prior slide

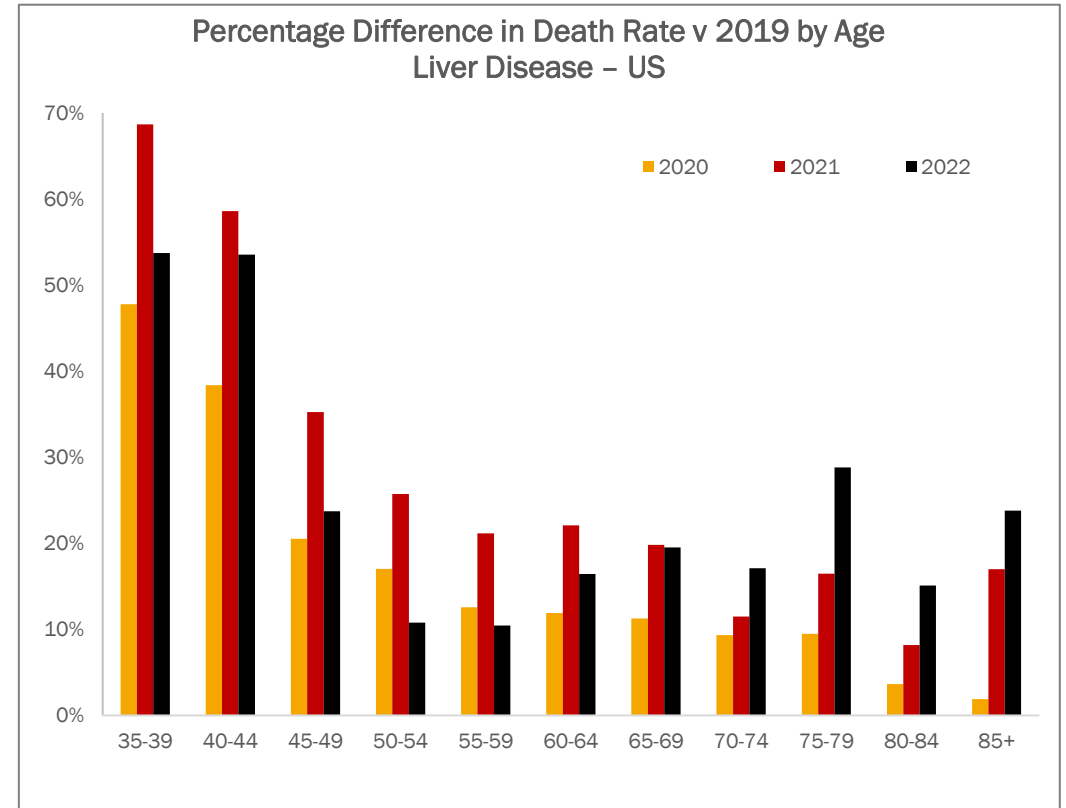
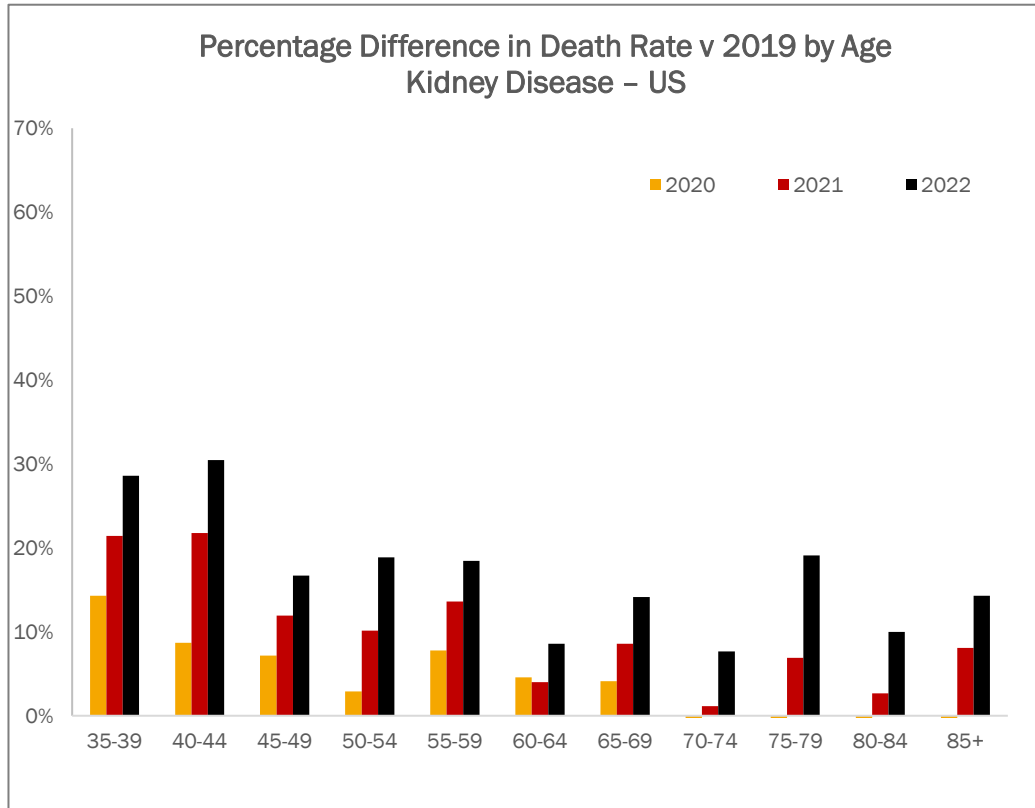


Source: CDC Wonder, data as of 3 Dec 2023, provisional data, primary cause of death. Note small numbers of deaths and/or data not available or not meaningful at younger ages.



Similar – but greater – rise in other notable pathologies (2/2)

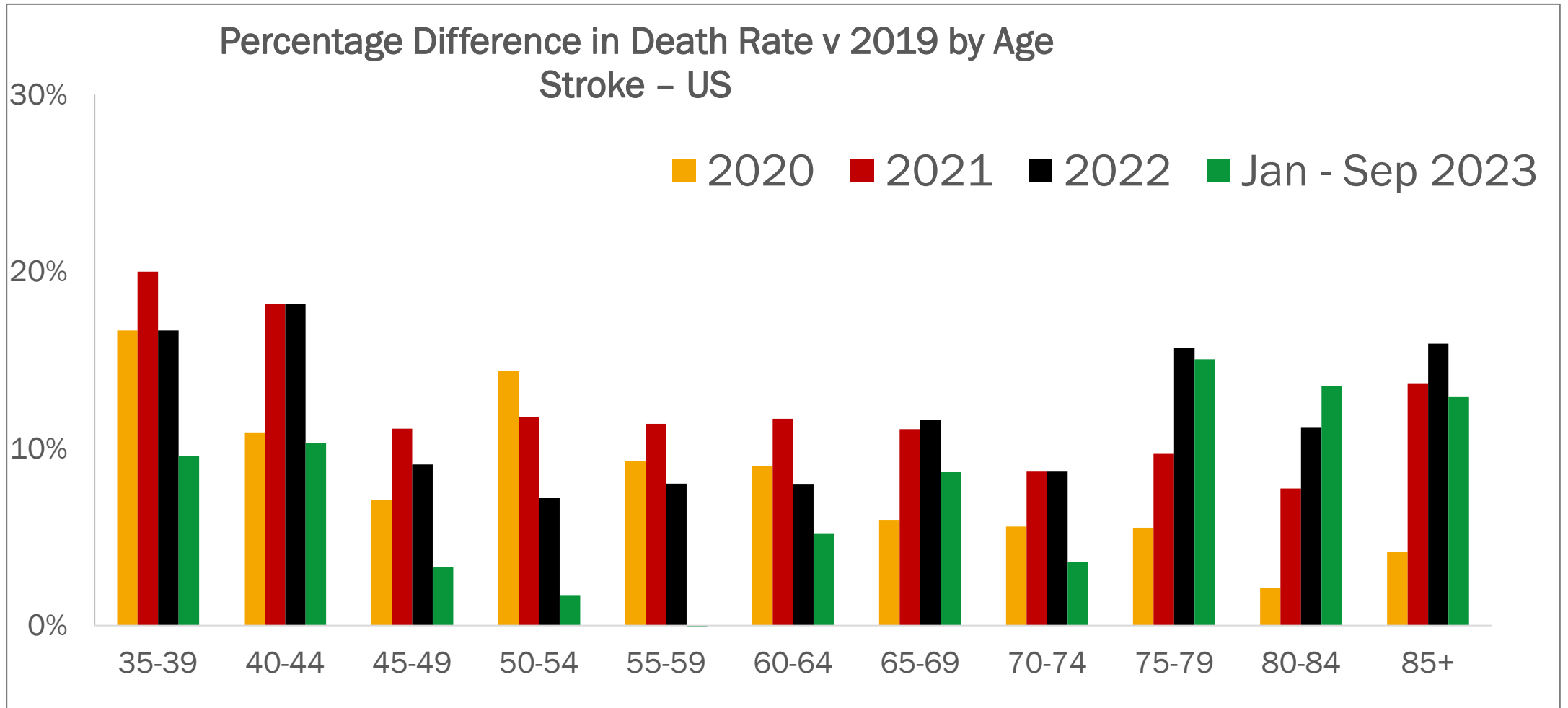
Note change in scale from prior slide



Source: CDC Wonder, data as of 3 Dec 2023, provisional data, primary cause of death. Note small numbers of deaths and/or data not available or not meaningful at younger ages.



Stroke deaths remain elevated in 2023, across many ages



Source: CDC Wonder, data as of 3 Dec 2023, provisional data, primary cause of death. Note small numbers of deaths and/or data not available or not meaningful at younger ages. Jan – Sep 2023 stroke deaths are compared against the same period in 2019.



Near-real-time German hospital data shows similar signals

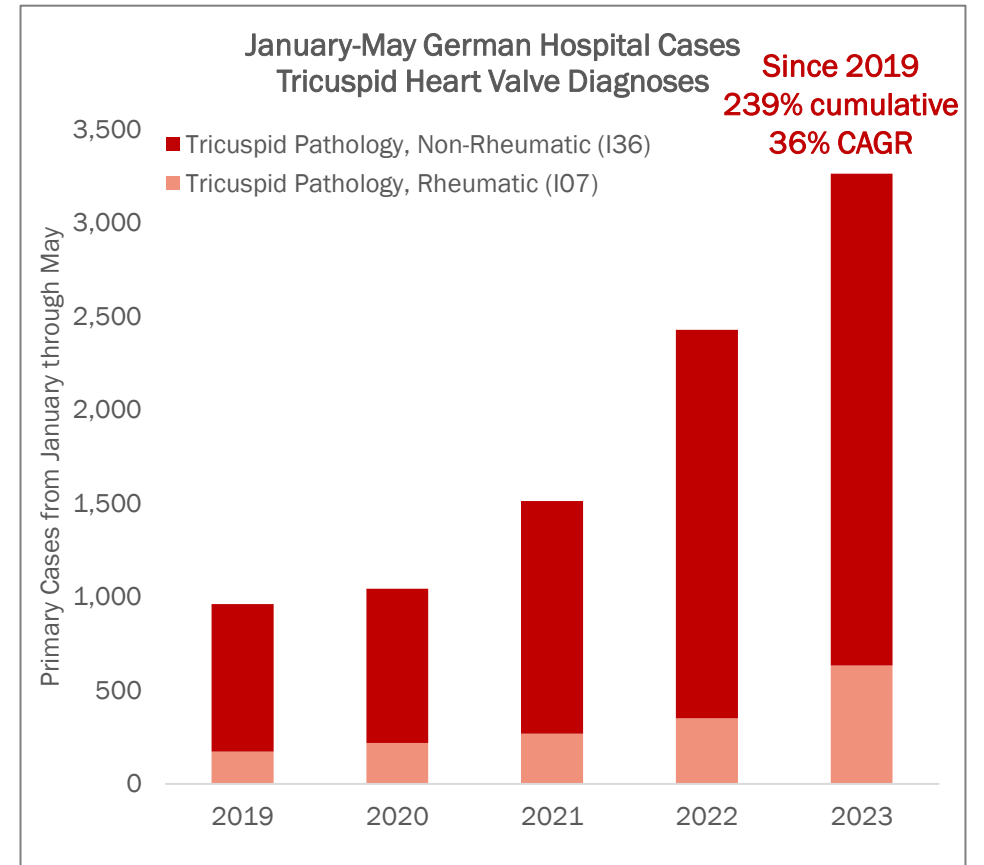
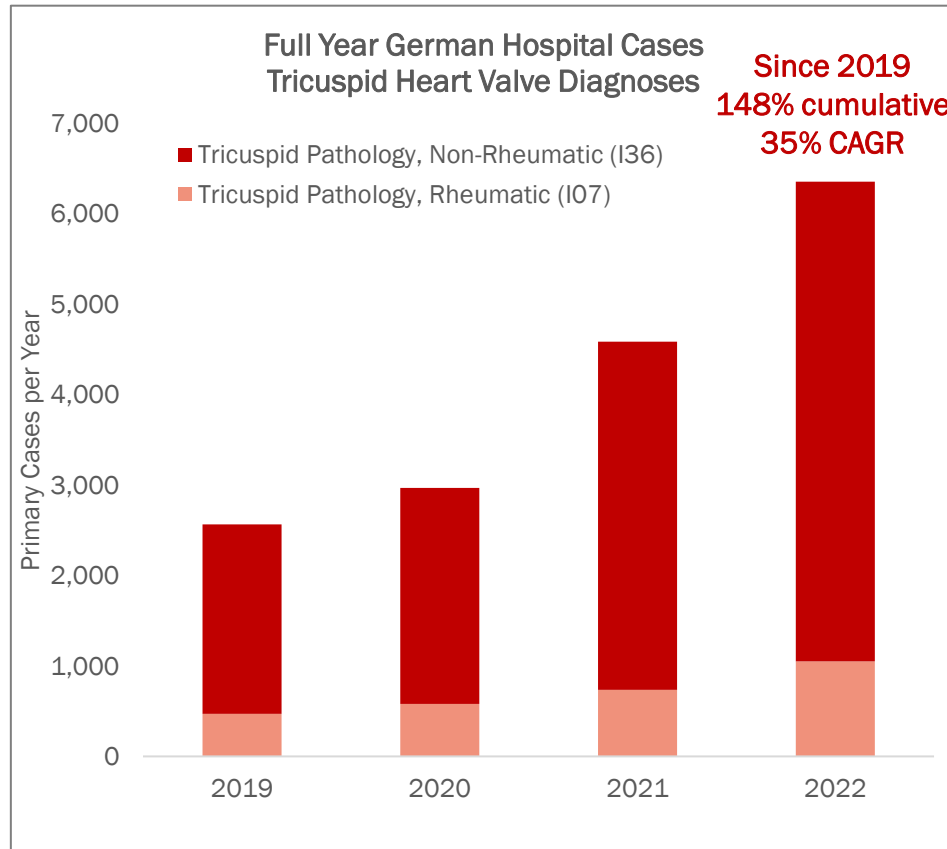
INEK German Hospital Data 2019-2022

All Chapters - Top 25 Primary ICDs By Most Elevated 2022 % Signal (Excluding Smallest ICDs)

ICD Sub-Chapter	ICD Sub-Chapter Description	ICD Code	ICD Description	2019	2020	2021	2022	P Value	2022 Cases	% of Total Cases	Excess Cases Est
Bacteria	A30-A49 Other bacterial diseases	A49	Bacterial infection of unspecified site	1.00	1.70	1.80	1.86	-	37,600	0.2%	17,434
& Virus	B25-B34 Other viral diseases	B33	Other viral diseases, not elsewhere classified	1.00	2.36	3.67	5.33	-	965	0.0%	784
	B25-B34 Other viral diseases	B34	Viral infection of unspecified site	1.00	1.12	1.68	2.66	-	35,562	0.2%	22,215
Cancer	C00-C97 Malignant neoplasms	C69	Malignant neoplasm of eye and adnexa	1.00	0.95	1.22	1.22	-	5,442	0.0%	995
	D00-D09 In situ neoplasms	D09	Carcinoma in situ of other and unspecified sites	1.00	1.11	1.17	1.24	-	3,784	0.0%	724
Metabolic	E65-E68 Obesity and other overeating	E66	Obesity	1.00	0.92	1.11	1.37	-	39,166	0.2%	10,572
	E70-E90 metabolic disorders	E88	Other metabolic disorders	1.00	1.17	1.60	1.85	-	4,719	0.0%	2,172
Behavioral	F50-F59 Behavioral problems with physical disorders and factors	F50	Eating disorders	1.00	0.98	1.40	1.26	-	4,003	0.0%	832
	F60-F69 personality and behavioral disorders	F64	Gender identity disorders	1.00	0.99	1.12	1.21	-	4,670	0.0%	803
	F80-F89 developmental disabilities	F84	Disruptive developmental disorders	1.00	0.90	1.24	1.22	-	1,205	0.0%	242
Heart	I05-I09 Chronic rheumatic heart diseases	I07	Rheumatic tricuspid valve diseases	1.00	1.23	1.57	2.24	-	1,054	0.0%	583
	I30-I52 Other forms of heart disease	I36	Nonrheumatic tricuspid valve disorders	1.00	1.14	1.84	2.53	-	5,303	0.0%	3,208
Lungs	J00-J06 Acute upper respiratory infections	J06	Acute upper respiratory infections of multiple and unspecified sites	1.00	0.82	0.73	1.39	-	53,004	0.3%	14,796
	J09-J18 influenza and pneumonia	J12	Viral pneumonia, not elsewhere classified	1.00	7.91	16.85	8.46	-	107,943	0.6%	95,190
	J95-J99 Other diseases of the respiratory system	J98	Other respiratory disorders	1.00	1.04	1.00	1.38	-	14,502	0.1%	3,980
Joints	M00-M25 arthropathies	M00	Pyogenic arthritis	1.00	1.07	1.13	1.21	-	17,396	0.1%	2,979
Maternal & Fetal	N80-N98 Non-inflammatory diseases of the female genital tract	N87	Dysplasia of cervix uteri	1.00	1.15	1.37	1.35	-	3,788	0.0%	975
	O94-O99 Other conditions of the gestational period not elsewhere classified	O98	Maternal infectious and parasitic diseases during pregnancy	1.00	0.52	0.62	1.18	-	6,385	0.0%	957
Other & Unknown	P80-P83 Disease states involving the skin and temperature regulation in the fetus and newborn	P81	Other disturbances of temperature regulation	1.00	1.01	1.12	1.34	0	559	0.0%	142
	R00-R09 Symptoms affecting the circulatory system and the respiratory system	R05	Cough	1.00	1.28	1.31	2.31	-	6,513	0.0%	3,693
	R50-R69 general symptoms	R50	Fever of other and unknown origin	1.00	1.10	1.18	2.28	-	17,446	0.1%	9,788
Misc	R50-R69 general symptoms	R53	Malaise and fatigue	1.00	0.82	1.00	1.72	-	14,522	0.1%	6,071
	Z00-Z13 People who use the healthcare system for examination and clarification	Z11	Special screening examination for infectious diseases	1.00	2.23	3.51	9.63	-	3,054	0.0%	2,737
	Z20-Z29 Individuals with potential health risks related to communicable diseases	Z22	Carrier of infectious disease	1.00	9.03	14.22	34.44	-	5,993	0.0%	5,819
COVID	Z80-Z99 Individuals with potential health risks based on family or personal history and certain conditions affecting health status	Z85	Personal history of infectious diseases	1.00	1.74	4.19	4.91	-	584	0.0%	465



148%+ rise in tricuspid heart valve disorders may be a signal





3 So what can we do?

**Insurers who lead
can save money,
and will save lives.**



Reflecting on continued elevated mortality & morbidity...

we had two simple insights

**By proactively testing
policyholders we can
identify those at risk for
adverse outcomes**

**By communicating results
and triaging to care
insurers can save money,
and save lives**



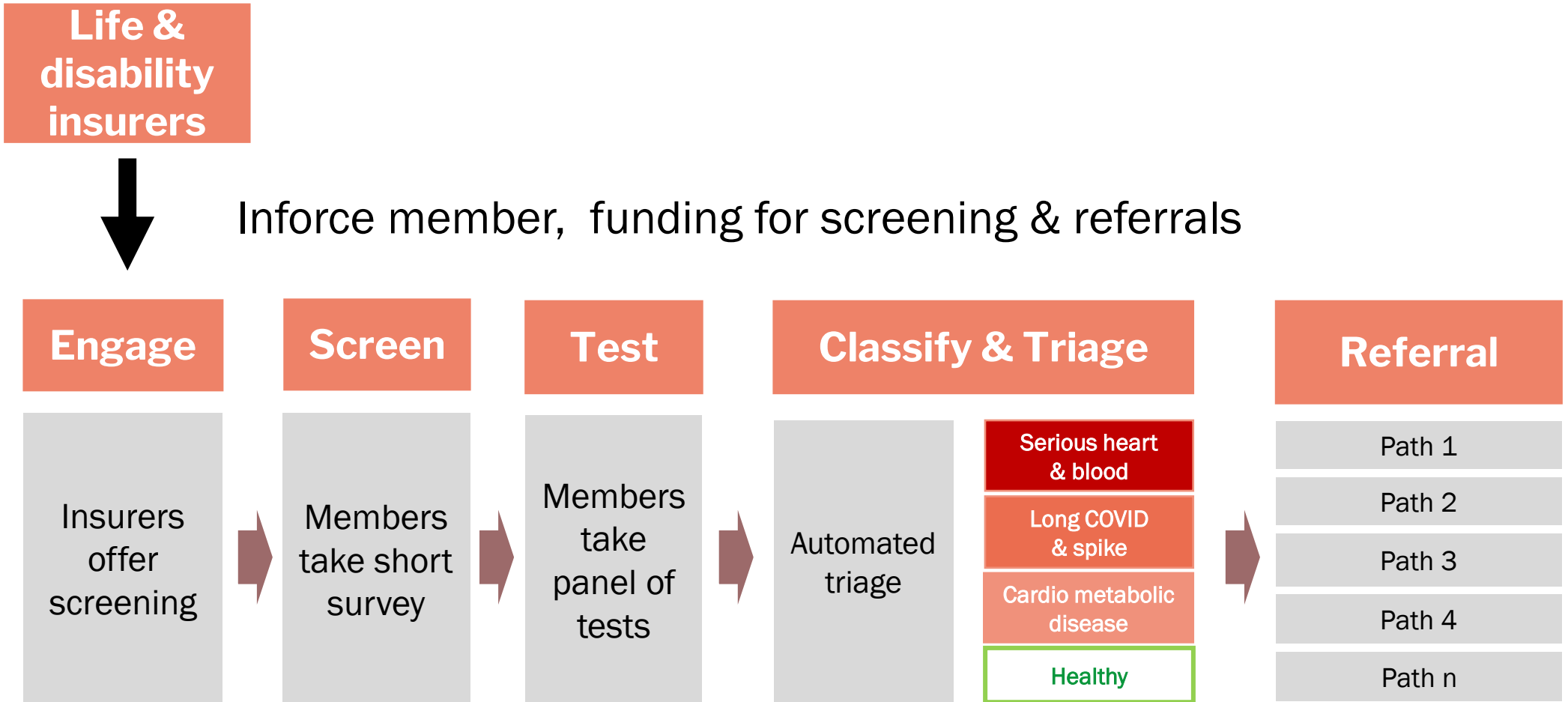
The solution? Insurers can

Screen, Test, & Triage

to save money, and save lives.



Proactive, targeted loss mitigation can be powerful



Proactive engagement to triage to care or lifestyle change can unlock value

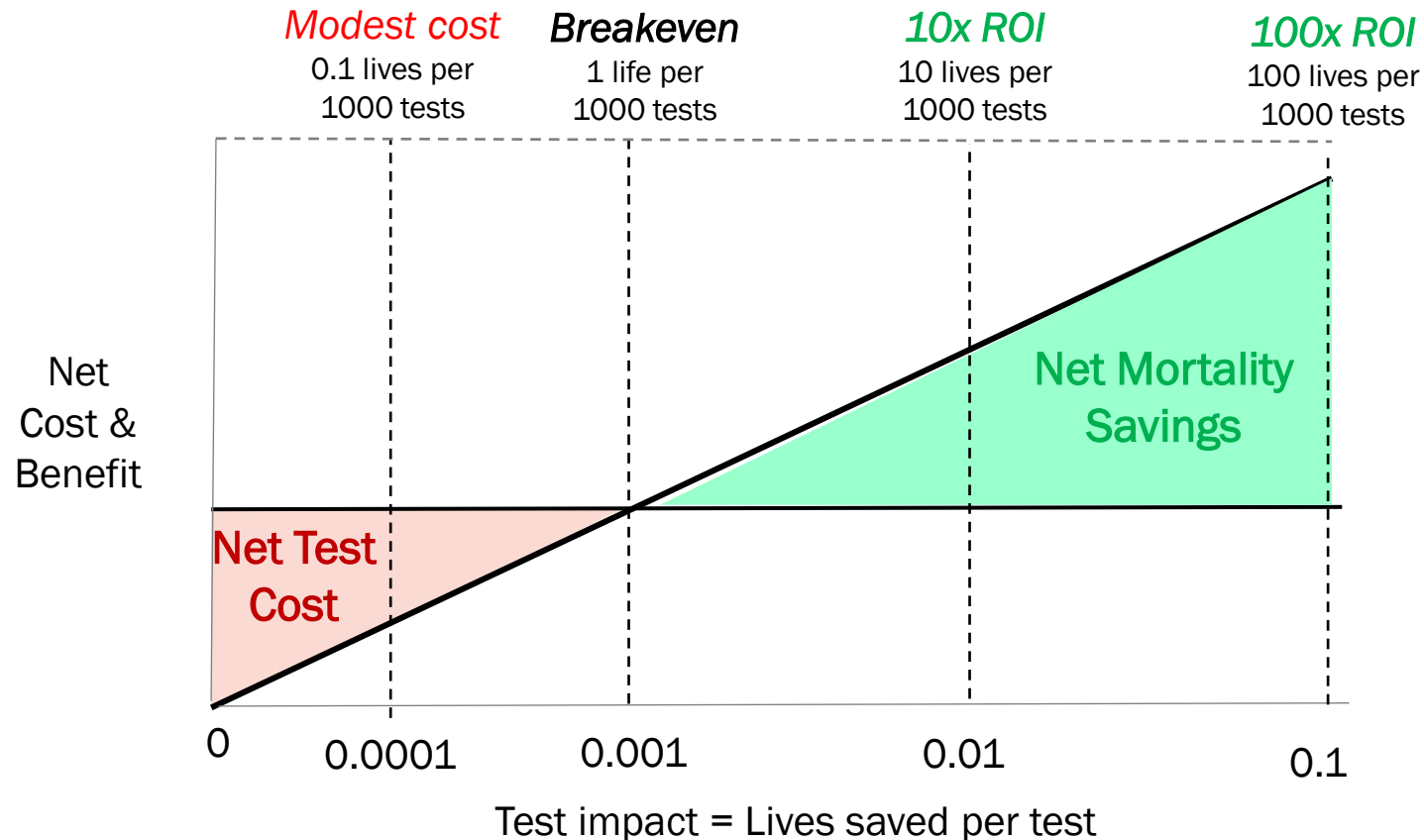


Potential returns from proactive risk mitigation are compelling

Sensitivity analysis shows low breakeven and large upside

And opportunity to

Net savings sensitivity for \$200k term policy and \$200 test panel cost



Reduce test panel cost to less than < \$100

Iterate policyholder engagement to improve efficacy

Target larger dollar policies to fund greater investment



Our approach is supported by medical research

High powered studies show biomarkers

...correlate with long-term all-cause mortality

and multi-variate models show large lift

Yang et al. *Journal of Translational Medicine* (2023) 21:471
https://doi.org/10.1186/s12967-023-04334-w

Journal of Translational Medicine

RESEARCH

Open Access



Development and validation of a blood biomarker score for predicting mortality risk in the general population

Jing Yang^{1†}, Jiayi Lu^{1†}, Junyan Miao¹, Jiacong Li¹, Meng Zhu^{1,2}, Juncheng Dai^{1,2}, Hongxia Ma^{1,2,3}, Guangfu Jin^{1,2} and Dong Hang^{1,2*}

Abstract

Background Blood biomarkers for multiple pathways, such as inflammatory response, lipid metabolism, and hormonal regulation, have been suggested to influence the risk of mortality. However, few studies have systematically evaluated the combined predictive ability of blood biomarkers for mortality risk.

Methods We included 267,239 participants from the UK Biobank who had measurements of 28 blood biomarkers and were free of cardiovascular disease (CVD) and cancer at baseline (2006–2010). We developed sex-specific blood biomarker scores for predicting all-cause mortality risk in a training set of 247,503 participants from England and Wales, and validated the results in 19,736 participants from Scotland. Cox and LASSO regression analyses were performed to identify independent predictors for men and women separately. Discrimination and calibration were evaluated by C-index and calibration plots, respectively. We also assessed mediating effects of the biomarkers on the association between traditional risk factors (current smoking, obesity, physical inactivity, hypertension, diabetes) and mortality.

Results A total of 13 independent predictive biomarkers for men and 17 for women were identified and included in the score development. Compared to the lowest tertile of the score, the highest tertile showed a hazard ratio of 5.36 (95% confidence interval [CI] 5.04–5.71) in men and 4.23 (95% CI 3.87–4.62) in women for all-cause mortality. In the validation set, the score yielded a C-index of 0.73 (95% CI 0.72–0.75) in men and 0.70 (95% CI 0.68–0.73) in women for all-cause mortality; it was also predictive of CVD (C-index of 0.76 in men and 0.79 in women) and cancer (C-index of 0.70 in men and 0.67 in women) mortality. Moreover, the association between traditional risk factors and all-cause mortality was largely mediated by cystatin C, C-reactive protein, 25-hydroxyvitamin D, and hemoglobin A1c.

Conclusions We established sex-specific blood biomarker scores for predicting all-cause and cause-specific mortality in the general population, which hold the potential to identify high-risk individuals and improve targeted prevention

Table S4. Associations of blood biomarkers with all-cause mortality for men and women in the training set

		Men		Women	
		HR (95% CI) ^a	P value	HR (95% CI) ^a	P value
CysC	Age-adjusted model	1.31 (1.29-1.34)	<0.0001	1.37 (1.34-1.41)	<0.0001
CRP	Age-adjusted model	1.31 (1.28-1.34)	<0.0001	1.29 (1.25-1.33)	<0.0001
GGT	Age-adjusted model	1.26 (1.24-1.29)	<0.0001	1.20 (1.17-1.23)	<0.0001
ALP	Age-adjusted model	1.22 (1.19-1.24)	<0.0001	1.16 (1.12-1.20)	<0.0001
HbA1c	Age-adjusted model	1.21 (1.19-1.23)	<0.0001	1.18 (1.15-1.21)	<0.0001
Glucose	Age-adjusted model	1.15 (1.13-1.17)	<0.0001	1.12 (1.09-1.15)	<0.0001
SHBG	Age-adjusted model	1.13 (1.11-1.16)	<0.0001	0.98 (0.95-1.01)	0.98
AST	Age-adjusted model	1.10 (1.07-1.12)	<0.0001	1.10 (1.07-1.14)	<0.0001
Calcium	Age-adjusted model	1.06 (1.04-1.08)	<0.0001	1.05 (1.02-1.08)	0.0007
TP	Age-adjusted model	1.05 (1.03-1.07)	<0.0001	1.05 (1.02-1.08)	0.0022
Phosphate	Age-adjusted model	1.03 (1.01-1.06)	0.0017	0.97 (0.94-1.00)	0.06
DBIL	Age-adjusted model	1.02 (0.99-1.04)	0.13	1.04 (1.00-1.07)	0.03
Urate	Age-adjusted model	1.02 (0.99-1.04)	0.06	1.18 (1.14-1.21)	<0.0001
TG	Age-adjusted model	1.01 (0.99-1.03)	0.48	1.13 (1.09-1.16)	<0.0001
ALT	Age-adjusted model	0.99 (0.98-1.02)	0.88	1.05 (1.02-1.09)	0.0007
Testosterone	Age-adjusted model	0.98 (0.96-1.00)	0.08	1.09 (1.05-1.12)	<0.0001
Creatinine	Age-adjusted model	0.96 (0.94-0.97)	<0.0001	1.03 (0.99-1.06)	0.06
TBIL	Age-adjusted model	0.91 (0.89-0.93)	<0.0001	0.94 (0.91-0.97)	0.0003
HDL-C	Age-adjusted model	0.91 (0.89-0.92)	<0.0001	0.84 (0.82-0.87)	<0.0001
ApoA1	Age-adjusted model	0.90 (0.88-0.92)	<0.0001	0.87 (0.84-0.89)	<0.0001
Urea	Age-adjusted model	0.90 (0.88-0.92)	<0.0001	0.99 (0.97-1.03)	0.94
ApoB	Age-adjusted model	0.88 (0.87-0.90)	<0.0001	0.93 (0.90-0.96)	<0.0001
FT	Age-adjusted model	0.88 (0.86-0.90)	<0.0001	1.08 (1.05-1.12)	<0.0001
IGF-1	Age-adjusted model	0.85 (0.84-0.87)	<0.0001	0.89 (0.86-0.92)	<0.0001
LDL-C	Age-adjusted model	0.85 (0.84-0.87)	<0.0001	0.89 (0.86-0.91)	<0.0001
TC	Age-adjusted model	0.85 (0.84-0.87)	<0.0001	0.86 (0.84-0.89)	<0.0001
ALB	Age-adjusted model	0.82 (0.80-0.84)	<0.0001	0.86 (0.83-0.88)	<0.0001
25(OH)D	Age-adjusted model	0.80 (0.78-0.81)	<0.0001	0.82 (0.79-0.84)	<0.0001

Abbreviations: HR, hazard ratio; CI, confidence interval; CRP, C-reactive protein; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; IGF-1, insulin-like growth factor-1; FT, free testosterone; SHBG, sex hormone-binding globulin; HbA1c, hemoglobin A1c; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; ALP, alkaline phosphatase; TBIL, total bilirubin; DBIL, direct bilirubin; TP, total protein; ALB, albumin; CysC, cystatin C; 25(OH)D, 25-hydroxyvitamin D.

^a HR per 1-SD increase in log-transformed biomarker concentration.

Table 1 (continued)

SD, standard deviation; BMI, body mass index; MET, metabolic equivalent; IQR, interquartile range; CRP, C-reactive protein; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; IGF-1, insulin-like growth factor-1; FT, free testosterone; SHBG, sex hormone-binding globulin; HbA1c, hemoglobin A1c; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; ALP, alkaline phosphatase; TBIL, total bilirubin; DBIL, direct bilirubin; TP, total protein; ALB, albumin; CysC, cystatin C; 25(OH)D, 25-hydroxyvitamin D.
^a The totals did not sum to 100% due to small proportions of participants choosing 'prefer not to answer'
^b 25(OH)D was adjusted for seasonality and calcium was adjusted for albumin

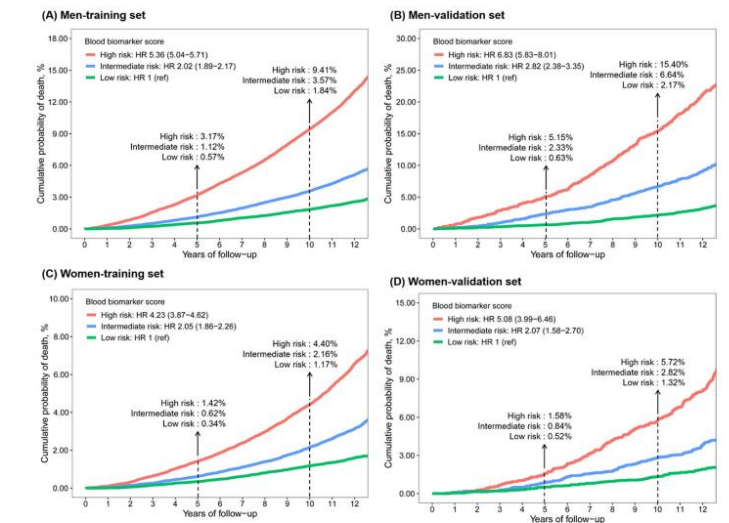


Fig. 1 Cumulative probability of death by tertiles of the blood biomarker score in the training and validation sets for men and women



We developed a prototype, we offered to our members

Cardiac & blood

Heart & kidney disease

Infection, immune & other

Inflammation

- hs CRP
- LP PLA2
- Myeloperoxidase

Injury

- D-Dimer
- Troponin, hs
- NT ProBNP

Event risk

- Homocysteine
- Lipoprotein (a)

Cardiometabolic disease

- Complete blood panel
- Lipids / Cholesterol panel
- Triglycerides / HDL
- Lipids fractional ion
- Glucose
- A1C
- Albumin
- Albumin/Creatine

Immune System & Other

- White blood cells
- Monocytes
- Monocytes/HDL
- Neutrophils/Lymphocyte
- Vitamin D
- COVID antibodies (quantitative)

Prototype panel developed through consultation with ICSSL's medical advisory committee & lab testing done by Quest Diagnostics and LabCorp



The biomarkers we selected are strong predictors of an **increase** or **decrease** in all-cause mortality, in numerous studies*

	Inflammation		Cardiac Injury		Cardiac Event Risk		
Sex	hsCRP	D-dimer	Troponin	NT ProBNP	Homocysteine	Lipoprotein A	
Male	+24%¹, +18%²						
Female	+19%¹, +6%²						
Combined	+35%³, +29%⁴		+24%⁴	+32%³	+46%³, +39%⁴	+22%⁴, +240%⁵ *	+9%⁶

	Cardiometabolic Disease				Immune System & Other				
Sex	LDL Size	UACR	A1c	TG	TG/HDL	Vitamin D	Monocytes / HDL	WBC	NLR
Male		-17%¹	+69%⁸, +10%¹	+6%⁹		-16%¹			
Female		-11%¹	+71%⁸, +3%¹	+34%⁹		-13%¹			
Combined	-26%⁷				+827%¹⁰ *	+57%¹¹ **	+19%¹²	+20%¹³	+44%¹⁴

Notes

Please see the following slide for study citations for studies 1-14.

* Selected models adjusted for sex, age, other health factors, & studied biomarkers, **not all are all-cause mortality (Homocysteine, TG/HDL)**

** **Low** vitamin D



Table of references

Referenced studies showing biomarkers' predictive capacity

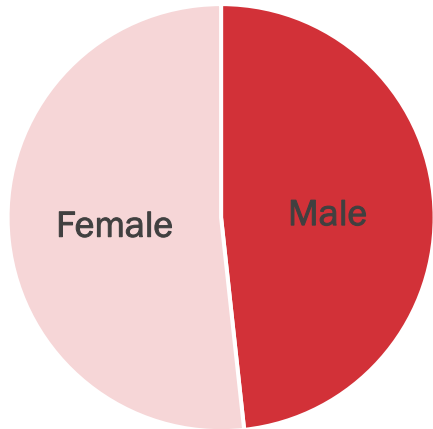
1. Yang et al. **Journal of Transl. Med.** (2023) 21:471
2. Singh-Manoux **CMAJ** 2017, M'13;1 89(10):E384-E390 *5 year/total study
3. Zehelius, et. al. **N Eng J Med** 2008:358:2107-16
4. Wang, et. al. **N Engl J Med.** 2006 D'21 355(25):2631-9
5. de Ruijter. et al. **BMJ 2009:** 338:a3083 * 85 y/old CVD mortality
6. Amiri. **N Eng J Med** 2008: European Journal of Epidemiology (2023). 38:485–499
7. Fischer, et. al. **PLoS Med** 11(2):e1001606 * If large
8. Caverro-Redondo , et. al. **BMJ Open** 2017:7:e015949. * Meta: >6.5/9% non/diabetic
9. Huang , et. al. **N Eng J Med** 2006; 355(25):2631-9
10. Hyang-Rae, et. al. **Clinica Chimica Acta.** 520 (2021) 29-33 *vs Framingham CVD risk score
11. Schottker , et. al. **BMJ** 2014:348:g3656 * if low
12. Jiang, et. al. **Lipids in Health and Disease** (2022) 21:30
13. Gillum , et. al. **Ann Epidemiol** 2005; 15:266–271
14. Gu, et. al. **Front. Cardiovasc. Med**, 12 May 2022



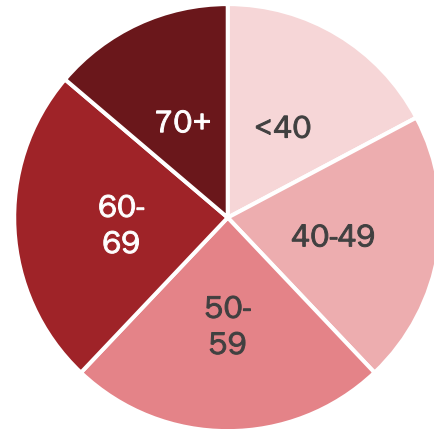
Our pilot was balanced by age, gender and health status

n = 29

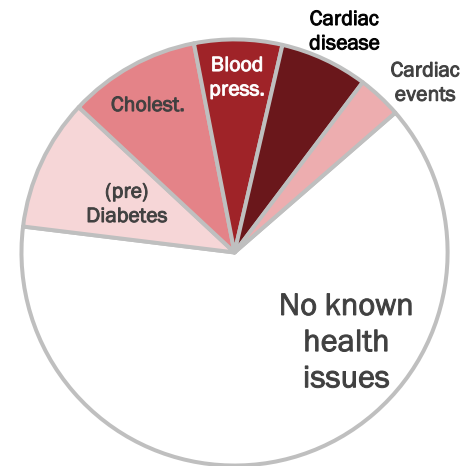
52% female



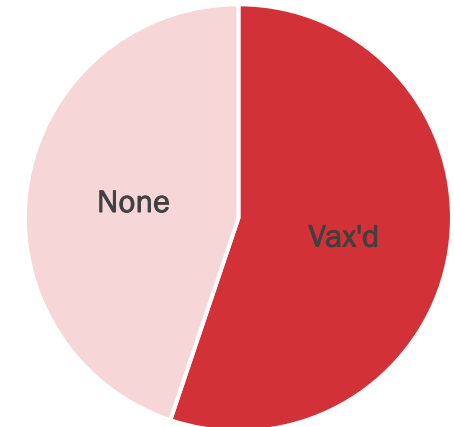
Average age 54



68% healthy



Majority vaccinated





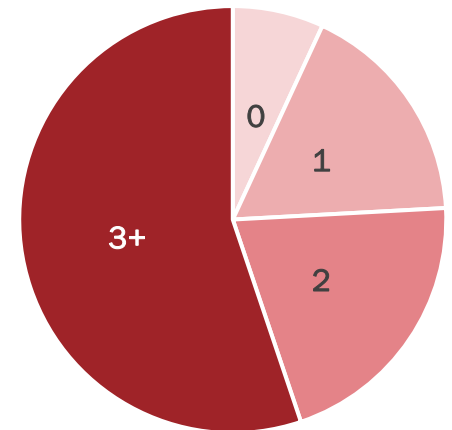
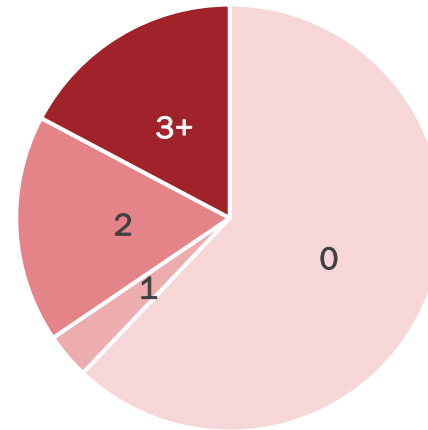
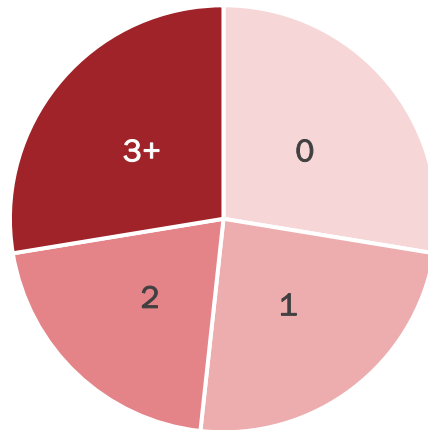
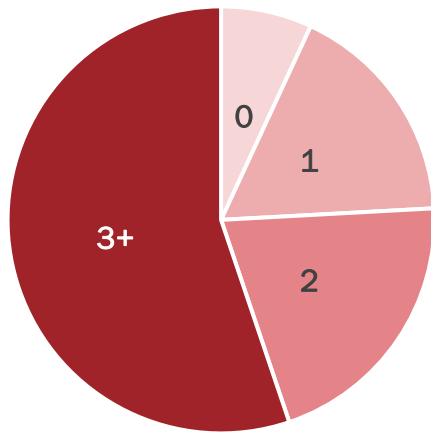
What we found: **93%** in our pilot had at least 1 abnormal result

93% have at least 1 abnormal result

76% more urgent blood and cardiac

38% long term heart & kidney disease

48% longer-term immune related

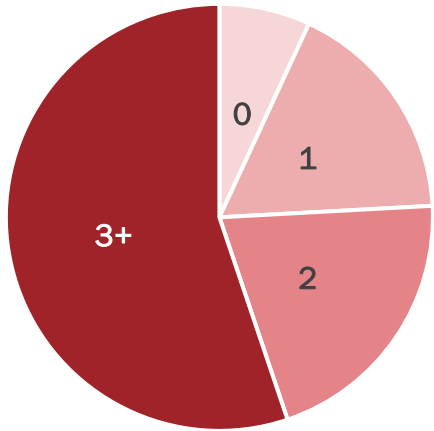


Note: #s are number of biomarkers determined "abnormal" per Quest Diagnostic and/or Healthmatters.io

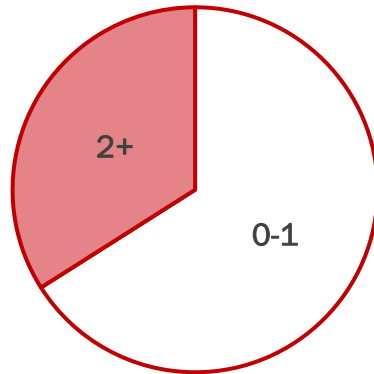


A majority had three or more abnormal markers

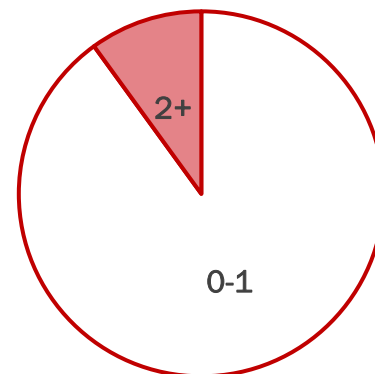
55% have 3+ abnormal markers



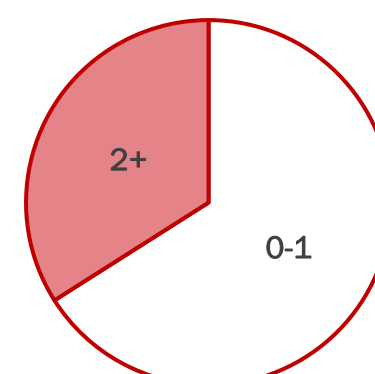
34% have 2+ cardiac findings



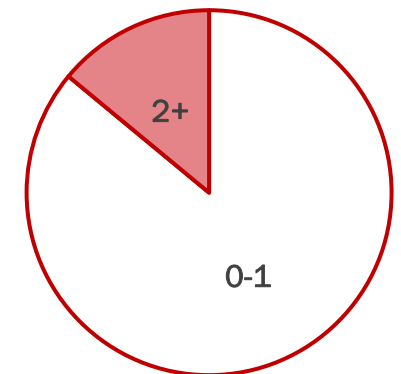
10% 2+ cardiac event risk findings



34% 2+ cardio & metabolic findings



14% 2+ immune findings



Note: #s are number of biomarkers determined "abnormal" per Quest Diagnostic and/or Healthmatters.io



All biomarkers had at least one finding, but some found many

Cardiac & blood

Heart disease & diabetes

Immune+

Inflammation

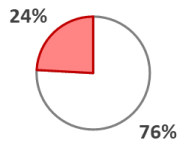
Injury

Event risk

Cardio-metabolic

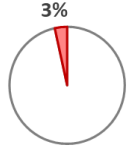
Immune & other

Inflammation
CRP, hs



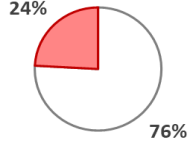
□ Inflammation CRP, hs

Inflammation
MPO



□ Inflammation MPO

Blood Clots - D-Dimer



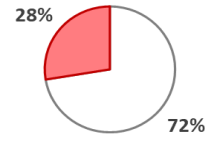
□ Blood Clots - D-Dimer

Cardiac Function
Loss - NT ProBNP



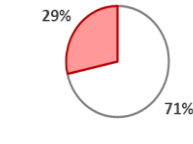
□ Cardiac Function Loss - NT ProBNP

Cardiac event risk
- Homocysteine



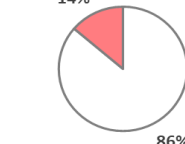
□ Cardiac event risk - Homocysteine

Cholesterol - LDL Size
Pattern



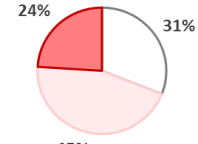
□ A Pattern Large Molecules = Good
■ B Pattern Small Molecules = Bad

Diabetes risk - high
A1C



□ Diabetes risk - high A1C

Vitamin D
Deficiency



□ Optimal □ Too low ■ Deficient

Abnormal White
Blood Cell %



□ Abnormal White Blood Cell %

Inflammation
LP PLA2



□ Inflammation LP PLA2

Cardiac Injury -
Troponin I, hs



□ Cardiac Injury - Troponin I, hs

Cardiac event risk -
Lipoprotein A



□ Cardiac event risk - Lipoprotein A

Diabetes - high
Albumin/Creatinine
Ratio



□ Diabetes - high Albumin/Creatinine Ratio

Cholesterol -
Triglycerides/HDL



□ Cholesterol - Triglycerides/HDL

Abnormal
Monocytes %

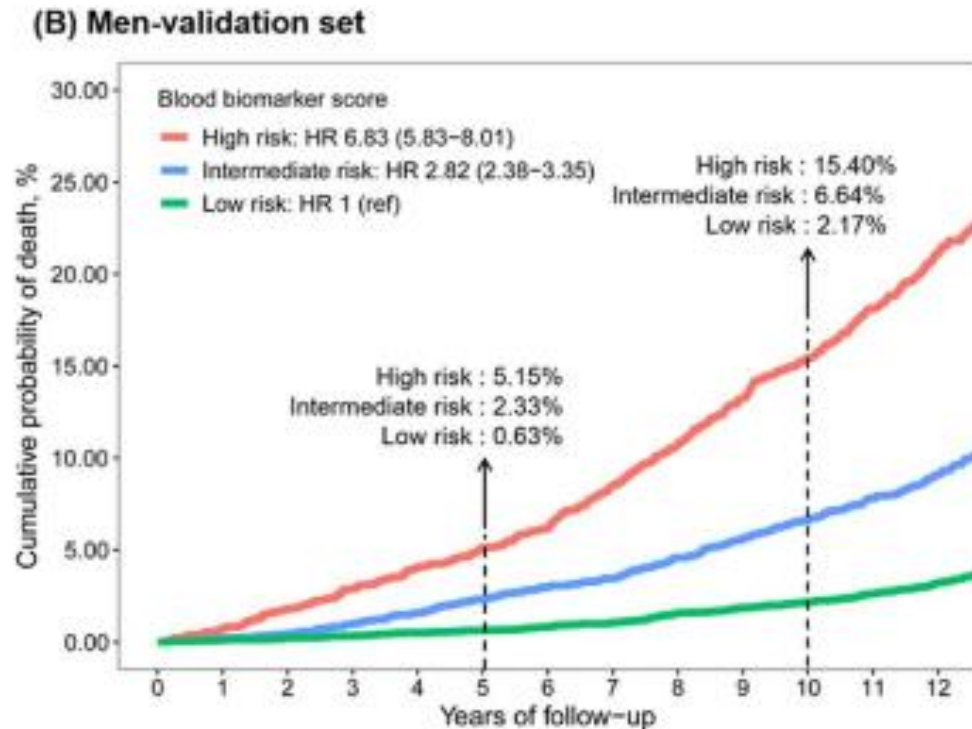


□ Abnormal Monocytes %



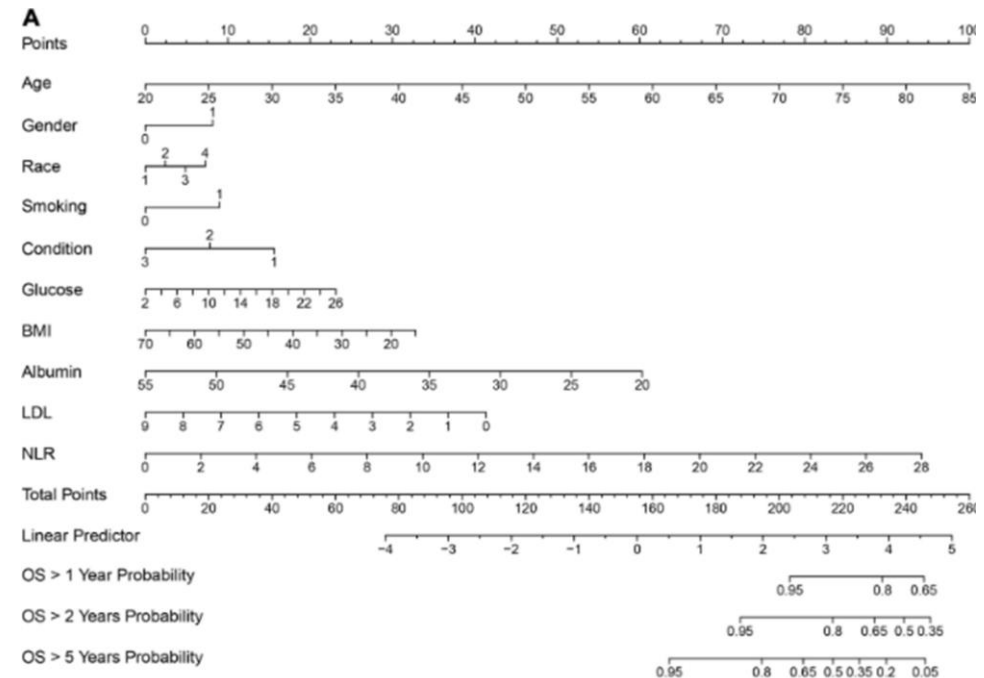
At scale, data science can power models to further optimize

Output from biomarker model – 7.5x lift



Development and validation of a blood biomarker score for predicting mortality risk in the general population Yang et al. *Journal of Translational Medicine* (2023) 21:471

Multi-factor risk calculator with AUC of 0.84



The Core Role of Neutrophil-Lymphocyte Ratio to Predict All-Cause and Cardiovascular Mortality: A Research of the 2005-2014 National Health and Nutrition Examination Survey Gu, et. al. *Front. Cardiovasc. Med.*, 12 May 2022



Our advisory team identified five risk profiles for intervention

Signs of possibly serious cardiac concerns

14% had 3+ markers of cardiac or circulatory inflammation or injury

This includes:
hs CRP (inflammation)
d-dimer (blood clots)
troponin/ntprobnp (injury)

Pilot data consistent with public data sets = possible widespread blood & cardiac issues

Identify and refer for medical diagnosis & care.

Presence of easily addressed cardiac event risk factor

28% had high Homocysteine, a risk-factor for heart attacks

Typically caused by vitamin deficiency (B6, B12, folic acid) and genetic factors

Homocysteine is toxic and significant contributor to heart attacks/stroke risk.

Identify those who need & send them B complex.

Presence of easily addressed immune risk factor

24% Vitamin D deficient and 69% were below optimal levels

Low levels of Vit. D worsen many immune, heart & other issues.

Most in U.S. need daily supplement of Vitamin D, some races, regions, seasons especially.

Identify those who need & send them Vitamin D..

Signs of lifestyle diseases & changes needed

17% had 3+ markers of heart or kidney disease

This includes:
TG/HDL, LDL size, A1C, glucose

Lifestyle diseases need lifestyle solutions, changes to diet, exercise, fasting, etc.

Provide coaching & apps for lifestyle change.

Signs of immune signals which may be COVID related

34% elevated monocytes, possibly related to C19

28% had very high C19 antibody levels (14x to 41x median).

Abnormally high antibodies may be proxy for acute, long, or other C19 risk, study is needed.

If unclear / long COVID symptoms are present, tests may help diagnose.

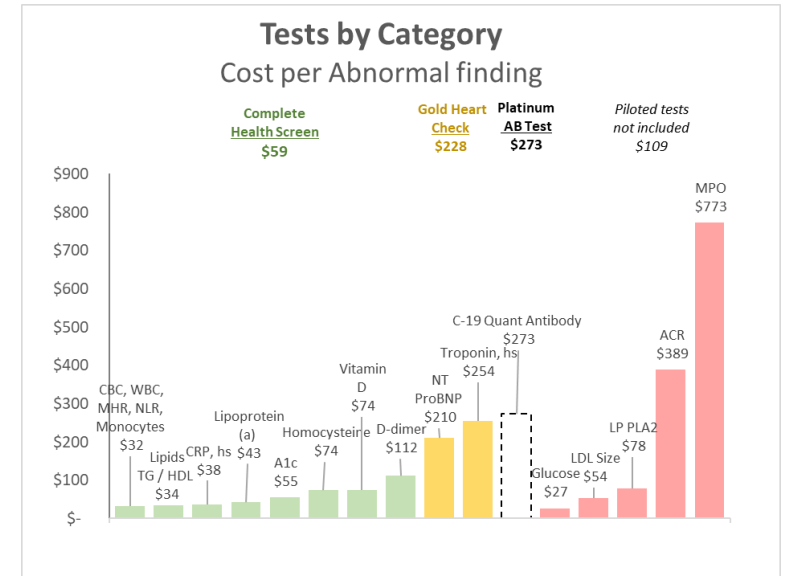
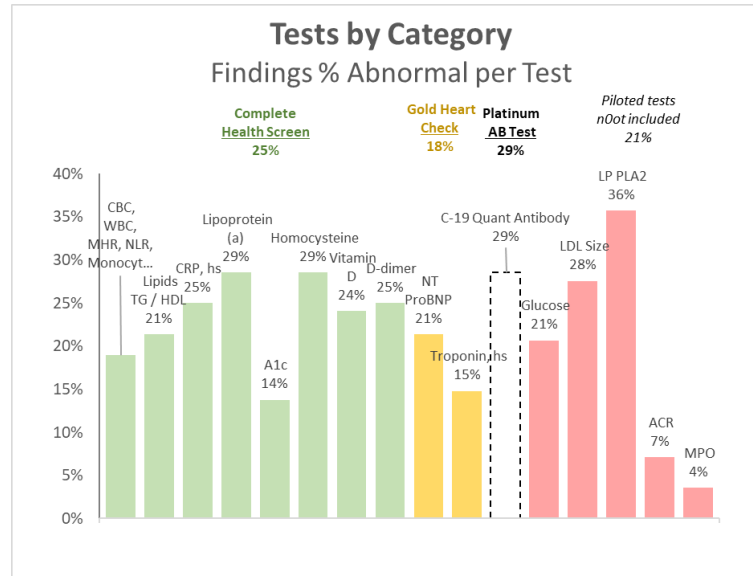
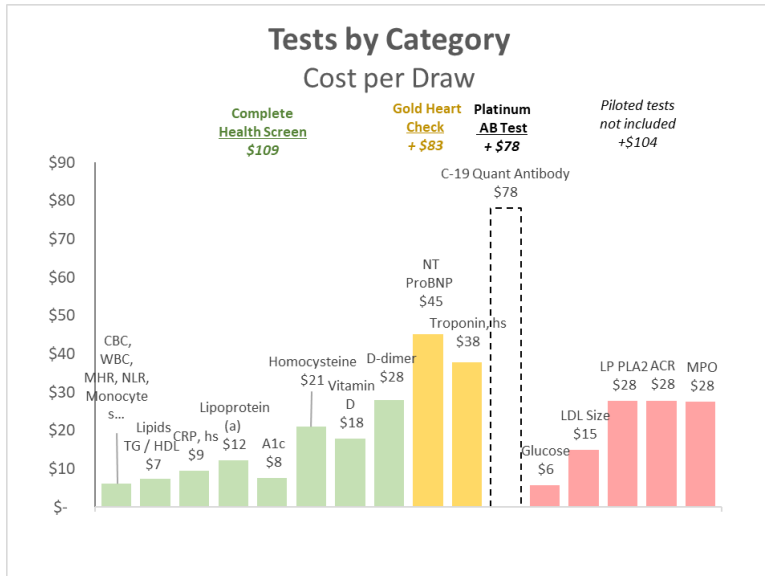


After pilot learnings, we developed a high impact ~\$100 panel

We created three packages...

...based on rate of findings

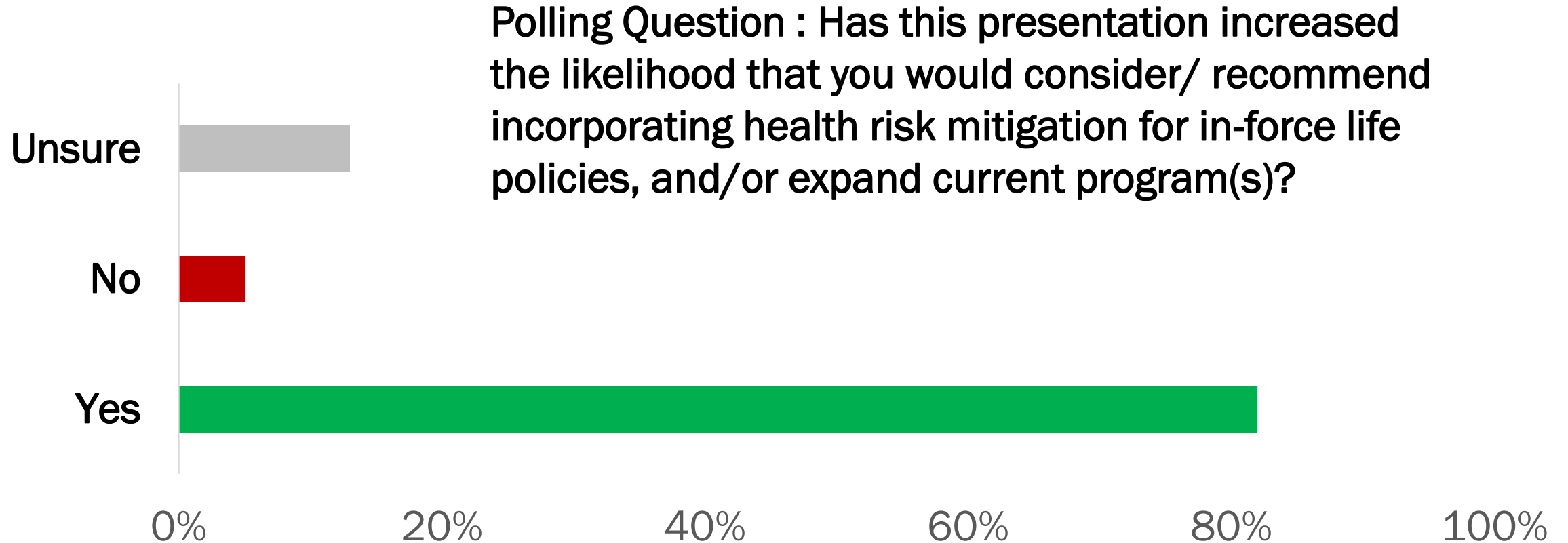
...balanced with cost



The Complete Health Screen will cost ~\$100, the Gold Heart Check ~\$175 and the Platinum C19 AB test ~\$250



We asked actuaries what they thought and were encouraged...





Let's return to the beginning : the three things to know

1

Younger adult mortality in U.S. is ~20% excess, in 2023 *

2

Morbidity analysis shows wide range of underlying conditions

3

Insurers who take steps to mitigate, can save money and will save lives

***and reported disability rate – a leading indicator of future mortality – is at all-time highs**



So where does this leave us?

1

Younger adult mortality in U.S. is ~20% excess, in 2023 *

The tragedy of elevated mortality and morbidity is real.

2

Morbidity analysis shows wide range of underlying conditions

Many pathologies and cardiac, circulatory & metabolic issues appear common

3

Insurers who invest in loss mitigation, can save money and will save lives

We found 1 in 7 w/ 3+ blood & cardiac risk markers.

A majority also had serious vitamin deficiencies

Insurers can find at risk for ~\$100 per test panel

Targeted care can reduce mortality and morbidity



Next steps

**Insurers who lead,
can save money,
and will save lives.**

We have great momentum but to save a million lives, we need your help – please join us today!



**Insurers who lead,
can save money,
and will save lives.**

Join us today.

Register to get our deck by email



Contact

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Insurance Collaboration to Save Lives

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book: calendly.com/josh-stirling-1

web: www.insurancecollaboration.org