ADM's APPLE:
The Accelerated Deaths Model with an Application to the Covid-19 Pandemic

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Agenda

- Objectives: understanding the Covid-19 pandemic
- The Proportionality Hypothesis
- Heterogeneity in mortality rates
- The Accelerated Deaths Model (ADM)
- Numerical examples
- Conclusions

Objectives

Questions asked at the start of the pandemic:

- Within a particular age group:
  which individuals were more likely to die from Covid-19 than others?
- What impact does this have on the average life expectancy of those who survive the pandemic? (⇒ *detrimental selection* effect)

In answering these questions we synthesize two strands of recent work:

- The Proportionality Hypothesis
  (Covid death rates underpinned by all-cause death rates by age and subgroup)
- Heterogeneity in death rates between subgroups and individuals

Covid-19 death rates and the Infection Fatality Rate (IFR)

At age x and for subgroup i (e.g. deprivation, ethnic background, urban-rural ...):

Cairns et al. (2024a): The Covid-19 death rate (annualised) can be written as

$$m_c(i,x) \equiv \tilde{IR}(i,x) IFR(i,x)$$

- $\tilde{IR}(i,x)$ = Infection Rate (annualised incidence rate)
- $IFR(i,x)$ = Infection Fatality Rate:

$$\begin{aligned}&\Pr\left(\text{Die from Covid} \mid \text{newly infected, age } x\text{, subgroup } i\right)\\ &= 1-\exp[-IFR(i,x)] \approx IFR(i,x)\end{aligned}$$

- Definition: Relative Frailty (RF)
  - $RF(i,x) \equiv IFR(i,x) \big/ m_A(i,x)$ where
  - $m_A(i,x)$ = pre-Covid all-cause death rate

The Proportionality Hypothesis: Cairns et al. (2024a)

- Hypothesis:
  $IFR(i,x)$ is approximately proportional to $m_A(i,x)$

- Equivalently:
  $RF(i,x)$ is approximately constant across all ages x and subgroups i

- But note: **Relative frailty does vary over time** due to
  # vaccinations, which vaccine(s), Covid variants, prior infections etc.

Heterogeneity and pandemic magnitude

Questions:

Q1: How much variation is there in all-cause death rates, $m_A(i,x)$,

- between subgroups
- within subgroups
- between individuals

$\longrightarrow$ heterogeneity

Q2: What is the right value for $RF(i,x) \equiv RF$ to generate the observed levels of deaths from Covid-19?

$\longrightarrow$ Pandemic *Magnitude* $\Rightarrow RF$

Heterogeneity in subgroup mortality: Cairns et al. (2024b)

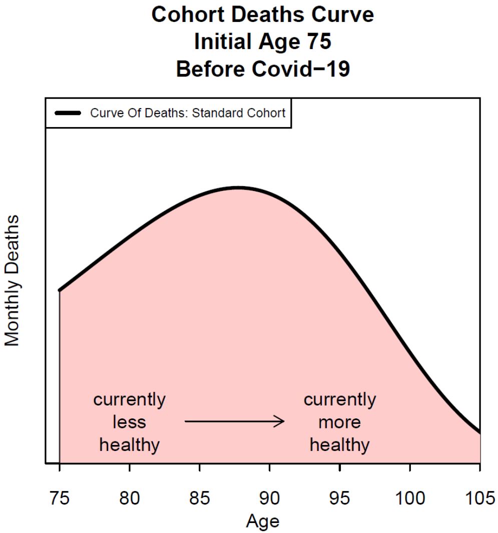
For a fixed age x: $m(x)$ = national all-cause death rate in a non-Covid year
subgroup i: $m(i,x)$ = all-cause death rate
For an individual j in subgroup i: $m_I(j,i,x)$ = all-cause death rate

- **Heterogeneity 1:** Death rates vary between subgroups due to:
  - Subgroup socio-economic characteristics (e.g. unemployment rates) (associative)
  - Prevalence of health risk factors (e.g. % of smokers, heavy drinkers,...) (causal)
  - Prevalence of multi-morbidities (even more causal!)
  - Controllable risk factors; non-controllable risk factors; random bad luck in disease onset
  - $m(i,x) = m(x) \times R_1(i)$
- **Heterogeneity 2:** Within each subgroup further variation between individuals
  - Individual variation in controllable risk factors versus subgroup average
  - Random bad luck in disease onset
    $\longrightarrow m_I(j,i,x)$ individual death rate for person j in subgroup i
- $m_I(j,i,x) = m(x) \times R_1(i) \times R_2(j,i) \quad = m(x)R(j,i)$ (*Biological frailty*)

The Accelerated Deaths Model (ADM)

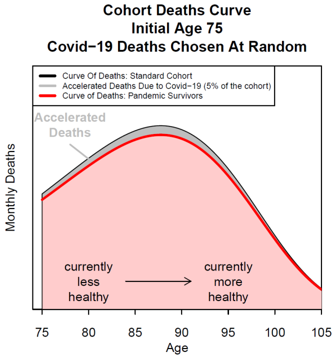
The ADM combines heterogeneity with the Proportionality Hypothesis to model the impact of Covid on life expectancies.

Pre-Covid: Cohort Curve of Deaths

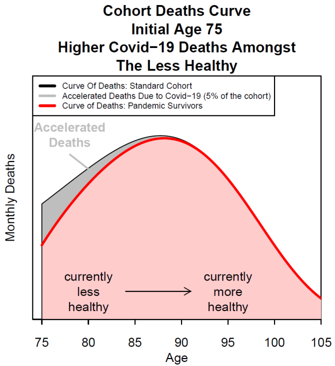


- For a cohort currently aged 75: what will be the distribution of ages at death?
- Notation: $d(t,x)$ = deaths at age $x+t$ from a cohort initially aged x
- Heterogeneity: Less healthy now ⇒ more likely to die sooner

Impact of Covid-19 on the Curve of Deaths



Cohort Deaths Curve
Initial Age 75
Covid−19 Deaths Chosen At Random



Cohort Deaths Curve
Initial Age 75
Higher Covid−19 Deaths Amongst
The Less Healthy

- Scenario A (left): Covid victims randomly chosen from the cohort
- Scenario B (right): Covid deaths more prevalent amongst the less healthy

Scenario B is consistent with the Proportionality Hypothesis

QUESTION: What is the right shape of the grey region?

The Accelerated Deaths Model (ADM)

We propose a simplified model to understand the impact of Covid-19 on future mortality rates:

- $\mu_B(t,x) =$ baseline death rates at age $x+t$ for a cohort initially aged x at time 0 (not directly observed!)
- $\mu(R,t,x) = R.\mu_B(t,x) =$ death rates for an individual or subgroup with relative risk R

Now introduce Covid (or other pandemic)

- Proportionality Hypothesis:
  Infection fatality rate, $IFR(i,x) \equiv \phi.\mu(R_1(i),0,x) = \phi.R_1(i).\mu_B(0,x)$
- $\phi =$ relative frailty
- $R_1(i) =$ subgroup i relative risk (non-Covid all cause)
- What is the full distribution of R?
  Subgroup → individual
  $R_1(i) \longrightarrow R(j,i) \equiv R_1(i).R_2(j,i)$

Survivor curves

- Given a relative risk of R: the survivor curve is then:

$$\begin{aligned} S(R,t,x) &= \exp\left[-\int_0^t \mu(R,s,x)ds\right] \\ &= \exp\left[-R\int_0^t \mu_B(s,x)ds\right] \\ \Rightarrow S(R,t,x) &= S_B(t,x)^R \end{aligned}$$

where the baseline survivor curve is $S_B(t,x) = \exp\left[-\int_0^t \mu_B(s,x)ds\right]$.

- BUT: $\mu_B(s,x)$ is not observed
- We do observe (or model) aggregate death rates and the aggregate survival curve:

$$S_A(t,x) = E\left[S(R,t,x)\right] = E\left[S_B(t,x)^R\right]$$

- Hence: $\mu_A(t,x)$ or $S_A(t,x)$ plus a distribution for the relative risk $R \Rightarrow \mu_B(t,x)$

Biological Frailty and Covid-19

- Cairns et al. (2024a) ⇒

$$\begin{aligned}\Pr(\text{die from Covid-19} \mid \text{newly infected with Covid-19}; \text{age } x; R) &= 1 - \exp\left[-IFR(R, x)\right] \\ &= 1 - \exp\left[-\phi R \mu_B(0, x)\right] \\ &\approx \phi R \mu_B(0, x)\end{aligned}$$

- R is the relative risk of an individual at the individual level
- ϕ is the relative frailty

Infections

- $\alpha(i,x) =$ proportion of group i infected with Covid-19.
- Assume $\alpha(i,x) = \alpha$ does not depend on i or x.
- $$\begin{aligned}\Pr(\text{die during the Covid-19 pandemic} \mid \text{age } x;\quad \alpha;\quad R) &= \alpha\left\{1 - \exp[-\phi R \mu_B(0,x)]\right\} \\ &\approx \alpha\phi R \mu_B(0,x)\end{aligned}$$
- Consequently, $\alpha\phi$ is the main driver of Covid mortality rather than α and ϕ individually.

Pandemic Magnitude

There are two very similar measures of magnitude:

- Magnitude #1 =
  in aggregate, proportion of a cohort that dies from Covid
  relative to aggregate pre-Covid all-cause death rate:

$$M_1(x) = \frac{\sum_{i,j} \alpha \left[1 - \exp\left\{-\phi R(j,i)\mu_B(0,x)\right\}\right]}{\sum_{i,j} R(j,i)\mu_B(0,x)} \quad \approx \alpha\phi$$

  $R(j,i)$ = simulated rel. risk for individual j in subgroup i

- Magnitude #2 = approximation to $M_1(x)$

$$M_2(x) \equiv \alpha\phi \quad \approx M_1(x)$$

- In our scenarios we input values of $M_2(x) \equiv M_2$ and α $\quad \Rightarrow \phi = M_2/\alpha$

Aggregate (national) mortality ⟶ Benchmark mortality curve

- National mortality: aggregate cohort mortality is assumed to follow the *Beard Law*
  (≈ Gompertz curve → upper limit)
  with an upper limit to the death rate of 0.5:

$$\mu_A(t,x) = \frac{a e^{b(x+t-x_0)}}{1 + a e^{b(x+t-x_0)}/0.5}.$$

- $x_0 = 60$, $a_0 = 0.006$, $b_0 = 0.09$: plausible/generic values
- Cohort Life Expectancy at age 60 ≈ 27 years
- $b_0 = 0.09$: $\Leftarrow$ a 'period' Gompertz rate of 0.1 less a mortality improvement rate of 0.01

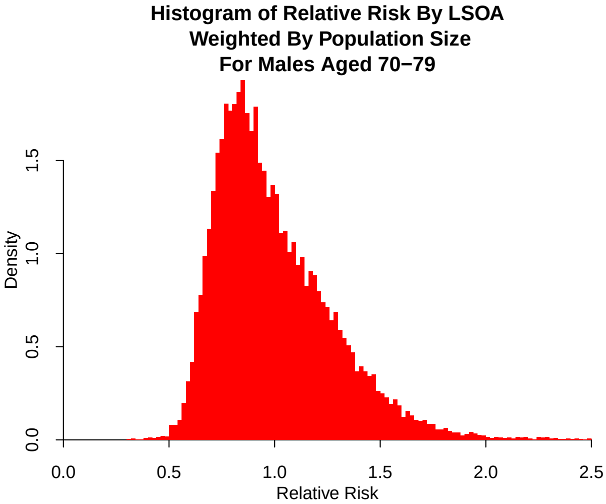
- (observed) $\mu_A(t,x)$ plus heterogeneity, $F_R(r) \Rightarrow \mu_B(t,x)$ (unobserved benchmark)

Numerical examples & sensitivity to key parameters

Scenario	M_2	σ	α	ϕ	a_0	a_1	b_0	b_1
A	2	0.4	0.2	10	0.006	–	0.09	–
B	2	0.8	0.2	10	0.006	–	0.09	–
C	2	0.4	0.8	2.5	0.006	–	0.09	–
D	2	0.8	0.8	2.5	0.006	–	0.09	–
E	0.4	0.6	0.2	2	0.006	–	0.09	–
F	0.4	0.8	0.2	2	0.006	–	0.09	–
G	0.4	0.6	0.8	0.5	0.006	–	0.09	–
H	0.4	0.8	0.8	0.5	0.006	0.006	0.09	0.09
I	0.4	0.8	0.8	0.5	0.006	0.006	0.09	0.0925
J	0.4	0.8	0.8	0.5	0.006	0.0063	0.09	0.09

- a_0, b_0: pre-Covid cohort mortality trajectory
- $a_0 \rightarrow a_1$: base table shifts up post-Covid
- $b_0 \rightarrow b_1$: improvement rate reduced post-Covid

Heterogeneity: the Log-normal assumption for relative risk R



- Cairns, Wen, Kleinow (2024b)
- 32844 small neighbourhoods (LSOAs)
- Each LSOA: similar socio-economic mix
- $R_1(i)$ = estimated relative risk for LSOA *i*
  relative to national death rates
- Observations are weighted by LSOA size
- Distribution is approximately log-normal(μ, σ^2)
- Data $\Rightarrow \sigma \approx 0.3$

Log-normal assumption for R

- R_1 = between subgroup variation $\sim \text{LogNormal}(-\frac{1}{2}\sigma_1^2, \sigma_1^2)$
- R_2 = within subgroup variation $\sim \text{LogNormal}(-\frac{1}{2}\sigma_2^2, \sigma_2^2)$

- $R = R_1 R_2 \sim \text{LogNormal}(-\frac{1}{2}(\sigma_1^2 + \sigma_2^2)\ ,\ \sigma_1^2 + \sigma_2^2)$

- Histogram $\Rightarrow \sigma_1 \approx 0.3$ above age 60

- England: no public data about σ_2 or $\sigma_1^2 + \sigma_2^2$
- So choosing σ_2 requires judgement

Pre- and post-Covid survivor curves and curves of deaths

- $S_A(t,x)$ = aggregate pre-Covid survivor curve
- $S_{AC}(t,x)$ = aggregate post-Covid survivor curve

- $S_{AC}(\mathbf{0},x) = 1$
- $S_{AC}(\mathbf{0}^+,x) < 1$: 0^+ means just after the pandemic
- $1 - S_{AC}(\mathbf{0}^+,x)$ = proportion who die from Covid

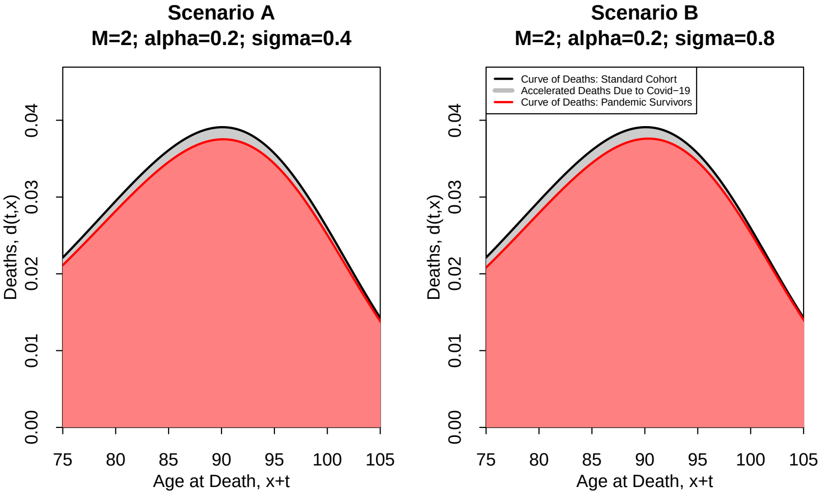
- $S_A(t,x) \longrightarrow d_A(t,x)$ aggregate pre-Covid curve of deaths
- $S_{AC}(t,x) \longrightarrow d_{AC}(t,x)$ aggregate post-Covid curve of deaths

$$\pi(t,x) = \frac{d_A(t,x) - d_{AC}(t,x)}{d_A(t,x)}$$

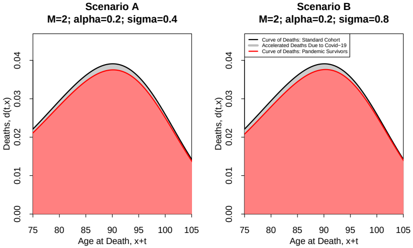
- $\pi(t,x)$ measures the impact of Covid on expected deaths at t

Examples: curve of deaths; age 75; High magnitude, $M_2 = 2$

Sensitivity to the heterogeneity parameter, $\sigma = 0.4 \rightarrow 0.8$

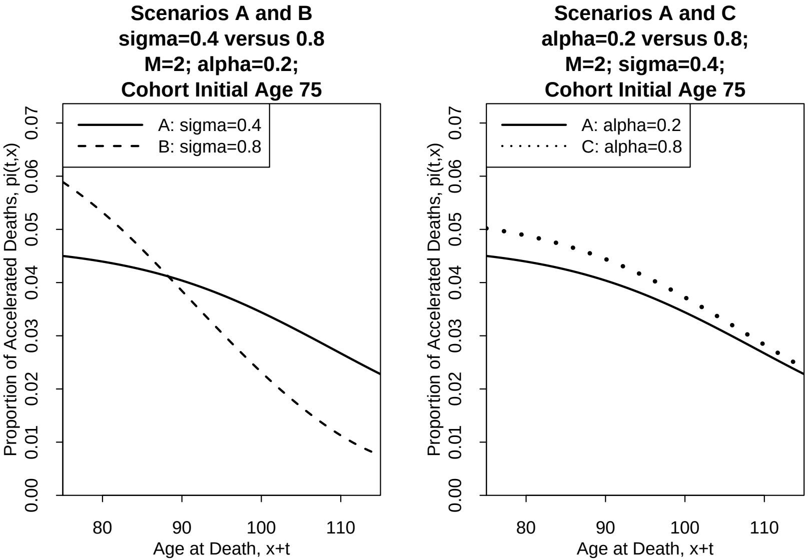


Examples: curve of deaths; age 75; High magnitude $M_2 = 2$

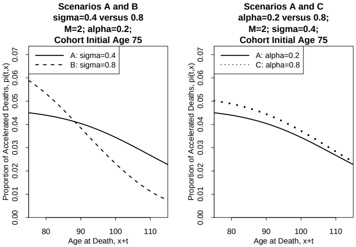


- The black line represents the pre-Covid curve of deaths for this cohort.
- The grey region represents the individuals expected to die at time t who actually die early due to or with Covid.
- The pink region represents the individuals who either weren't infected with Covid or who survived infection.
- In the two plots all parameters are the same except for $\sigma = 0.4$ or 0.8: less or more heterogeneity in biological frailty
- In spite of the big difference in the values of σ, the two plots are fairly similar.
- However, on closer inspection, in the right-hand plot, the grey region is more skewed to the left.

Examples: $\pi(t,x)$; age 75; Magnitude $M = 2$; Vary σ and α



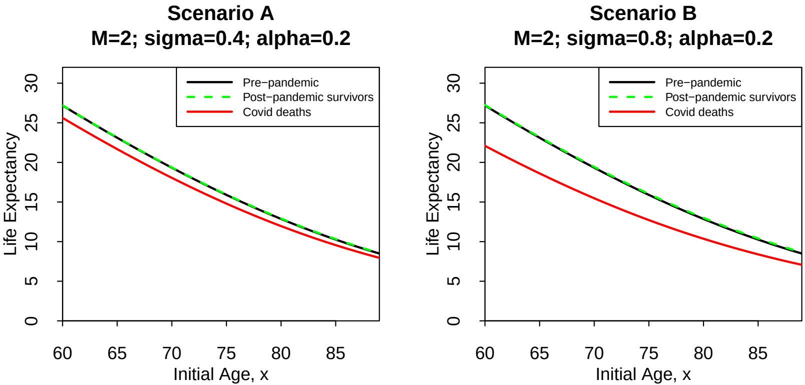
Examples: $\pi(t,x)$; age 75; Magnitude $M = 2$; Vary σ and α



- $\pi(t,x)$ is the derived proportion of those expected to die at t who die from Covid.
- **In the original 2020 paper $\pi(t,x)$ was modelled explicitly as an exponential curve declining to zero.**

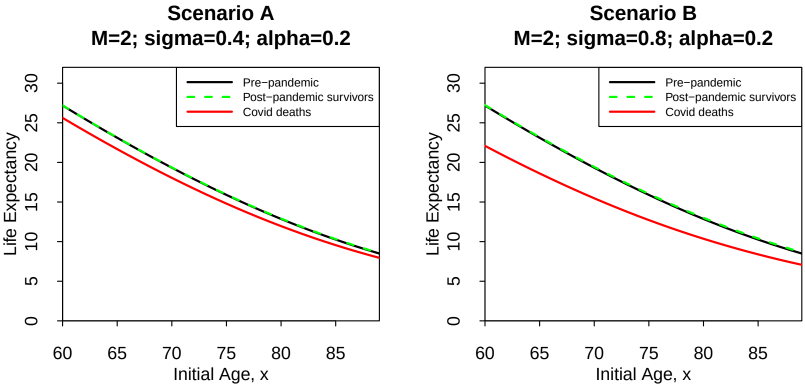
  (Cairns, Blake, Kessler and Kessler (2020) The Impact of Covid-19 on Future Higher-Age Mortality.)
- New model: $\pi(t,x)$ has a (reverse) sigmoid shape that declines to a positive limit.
- Increasing σ has a big impact – TILT; Covid deaths shift to the left
- Increasing α has a smaller impact – linked to the linear approximation to exponential; bigger impact at high ages, when the linear approximation is less good
- If magnitude M_2 is smaller, the impact of changing α is smaller

The Adjusted Post-Pandemic Life Expectancy (APPLE) and other LEs



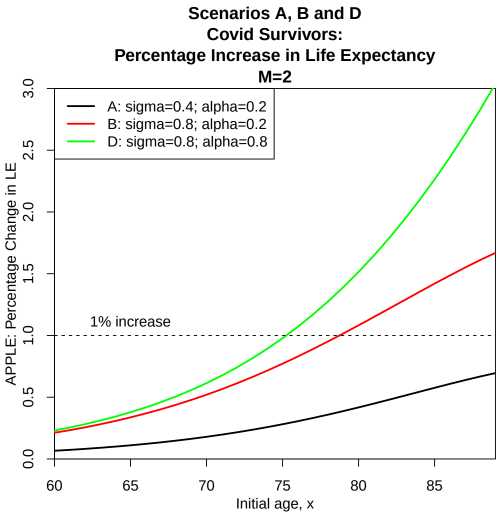
- — $LE(x)$ = (aggregate) mean pre-pandemic life expectancy
- — $YLL(x)$ = mean years of life lost by those who die with/from Covid
- - - $APPLE(x)$ = mean life expectancy of those who survive the pandemic

The Adjusted Post-Pandemic Life Expectancy (APPLE) and other LEs



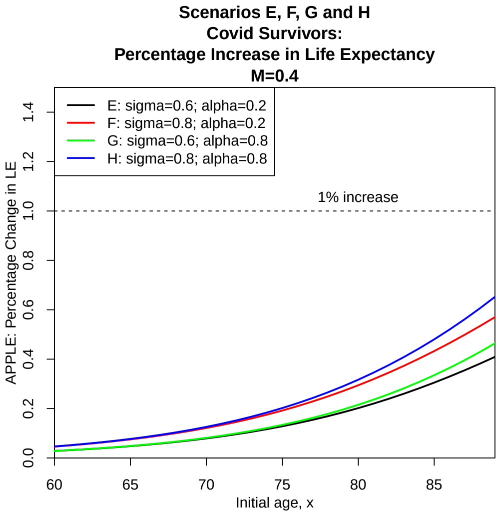
- Scenario A to B: increase σ
- The pre-pandemic $LE(x)$ and the $APPLE(x)$ appear almost the same
- $YLL(x)$ is well below $LE(x)$: those who die are much less healthy than the pre-pandemic average
- $YLL(x)$ is very sensitive to changes in heterogeneity, σ

APPLE versus Pre-Covid LE: High magnitude $M = 2$



- $100 \times (APPLE(x) - LE(x))/LE(x)$
- The % increase is quite small,
  but heavily age dependent
- Doubling σ more than doubles the % increase in LE, but the impact is fairly consistent across all ages.
- Changing from $\alpha = 0.2$ to 0.8 is more complex

Realistic scenario: APPLE versus Pre-Covid LE: $M = 0.4$

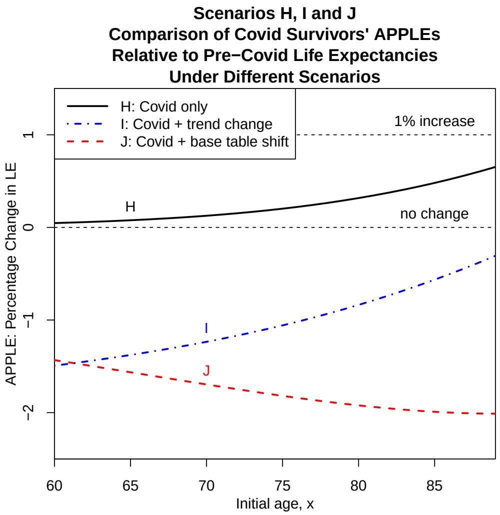


- $M = 0.4$ is consistent with *total* Covid deaths in England (2020-2023)
- Lowering $M \Rightarrow$ smaller % increase from LE to APPLE
- Results are less sensitive to choice of α
- σ is still a key driver

  $\Rightarrow$ assessing levels of heterogeneity is very important.
- Data for LSOAs gives us a lower bound for σ.

  But we don't know how much variation there is at the individual level within an LSOA.

Additional impact of a change in base table or improvement rate



- Scenario H: as before $M = 0.4$, $\sigma = 0.8$, $\alpha = 0.8$
- Scenario I: As scenario H but, post-Covid, **mortality improvement rates** are 0.25% lower per annum than pre-Covid assumptions
- Scenario J: As scenario H but, post-Covid, a permanent 5% increase in the **base table**
- Scenarios I and J both cause LEs to fall
- At younger ages, the impact is much bigger than the impact of Covid itself
- The gap between scenarios H and I narrows with age as the change in improvement rate has less time to have an impact.
- Conclusion: the detrimental selection effect due to Covid (scenario H) is much smaller than the disruptive impact of Covid on base tables and future improvement rates.

Conclusions

- A novel combination of the Proportionality Hypothesis + improving knowledge about mortality heterogeneity
  ⇒ a more accurate assessment of the impact of *detrimental selection* on life expectancies due to Covid.
- The impact of *detrimental selection* as a result of Covid infection might, in fact, be less than conjectured in Cairns et al. (2020)
- The impact of *detrimental selection* due to Covid is potentially much smaller than the potential impact of a step-change in base-table assumptions or a change in the assumed long-term improvement rate.

Conclusions (cont.)

- The results here indicate that having a good assessment of levels of heterogeneity in cohort mortality rates is very important.
- To refine our assessments of heterogeneity at the LSOA level we need to access individual level datasets. Individual datasets need to contain sufficient information about each individual to allow a assessment of each individual's probability of death over a given time horizon.
- Beyond the Covid pandemic there are lessons to be learned about heterogeneity and other diseases.
  - In a different form, heterogeneity also affects (a) the onset of both chronic and acute diseases and (b) an individual's ability to fight disease once established.
  - Potentially, this helps explain why (a) younger people are more likely to survive an acute illness (e.g. Covid) and (b) younger people are likely to experience a longer period of poor health before dying than older people.
- Applications:
  Future pandemics; excess winter mortality; life insurance + pensions; long term care insurance

Thank you

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- Paper: coming soon