# Covid-19:
# The Proportionality Hypothesis Revisited

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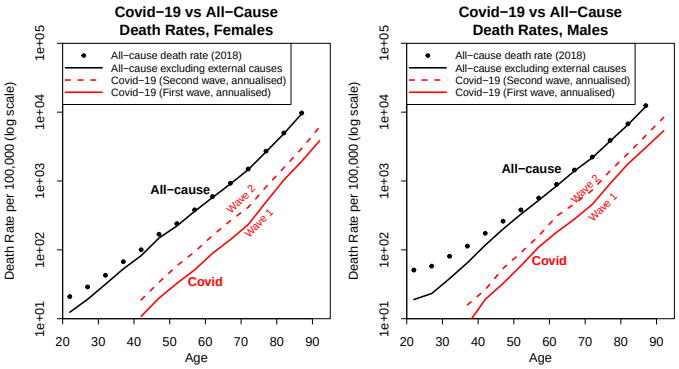
# Outline

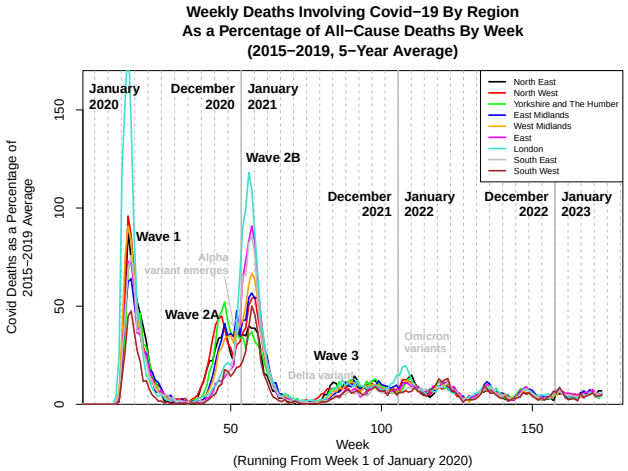
- What is the link between Covid-19 death rates and all-cause mortality?
- The three phases of Covid-19:
  initial pandemic/pre-vaccination phase; vaccination phase; endemic phase
- The Proportionality Hypothesis
- Testing the Proportionality Hypothesis
- Non-Covid excess deaths in the endemic phase

# Covid-19 Death Rates, Waves 1 and 2 (up to January 2021)



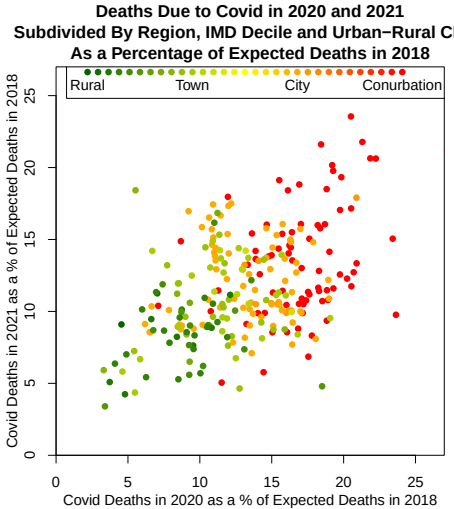

- Death rates are on a logarithmic scale
- All cause: with and without external causes
- Wave 1: March to August 2020
  Wave 2: September 2020 to February 2021
- Waves 1, 2 and 2018-all-cause are almost parallel!
- Waves 1 & 2: very similar age profile
- Conclusion: Covid death rates by age are approximately proportional to all-cause mortality (excluding external causes).

# Weekly Covid-19 Death Rates: 2020-23 by English Region




- Considerable variation between regions
- Wave 1: synchronised
  - London leads, but similar timing
  - Very different magnitudes
- Wave 2: not synchronised
  - Wave 2A more focused in the northern regions
  - Wave 2B stronger in the south
- Endemic phase: synchronised

# Covid Deaths in 2020 and 2021 as a Percentage of All Deaths in 2018




- Data: Annual Covid deaths for 6791 medium-sized neighbourhoods grouped by
- 9 regions ($r$) $\times$ 10 deprivation deciles ($i$) $\times$ 4 urban-rural classes ($u$)
- Compare Covid-19 deaths in 2020/2021 with deaths from all causes in 2018
- $D(\text{covid}, r, i, u, \text{year})/D(\text{all}, r, i, u, 2018)$
- Covid-19 deaths: 3% to 27% of 2018 deaths
- Moderate correlation between 2020 and 2021
- Rural $(r, i, u)$ subgroups have much lower Covid death rates than urban
- Implication: we also need to take account of infection rates

# The Subgroup Proportionality Hypothesis: Phase 1 of the pandemic

Covid mortality in the pre-vaccination phase depends on: age; socio-economic group; and other factors.

$$\text{Covid Death Rate}(i,x) \equiv \text{All-cause death rate}(i,x) \times \text{infection rate}(i,x) \times \text{relative frailty}(i,x)$$

$$m_C(i,x) = m_A(i,x) IR(i,x) RF(i,x)$$

E.g. $i \Rightarrow$
region; urban/rural; neighbourhood deprivation; ethnic group etc.

**Subgroup Proportionality Hypothesis:**
relative frailty$(i,x)$ does not vary much by age or sub-group

# The Subgroup Proportionality Hypothesis: Phase 1 of the pandemic

Related concept: the chances of dying from Covid-19 given infected

$$\text{Infection Fatality Rate}(i,x) = \text{All-cause death rate}(i,x) \times \text{relative frailty}(i,x)$$

$$IFR(i,x) = m_A(i,x)RF(i,x)$$

**Subgroup Proportionality Hypothesis** $\Rightarrow$
For each subgroup $i$: $IFR(i,x)$ is approx. proportional to $m_A(i,x)$

Support for the hypothesis:

- Covid mortality by age almost parallel to all-cause mortality by age
  $\Rightarrow$ hypothesis holds across ages
- Antibody survey data for Wave 1
- ONS data for deprivation deciles and 9 regions
  $\Rightarrow$ hypothesis holds across (deprivation) subgroups

# The Aggregate Proportionality Hypothesis

- Whole of England; no subgroups

$$m_C(x) = m_A(x)IR(x)RF(x)$$

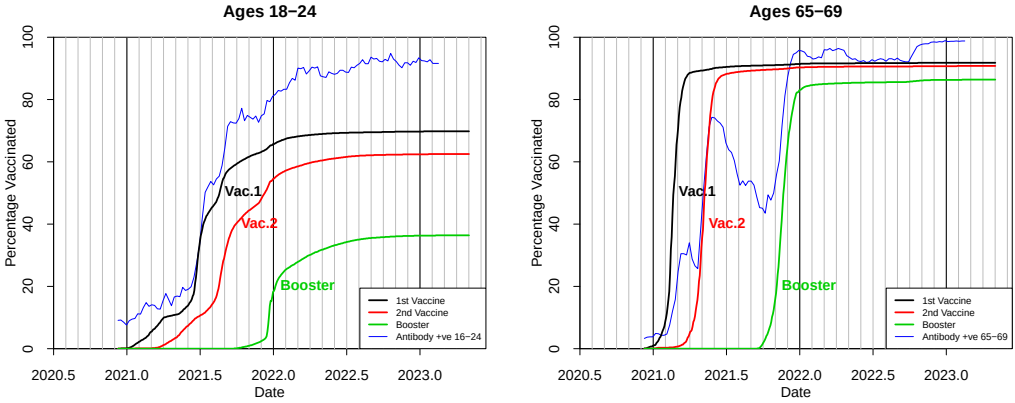
$$IFR(x) = m_A(x)RF(x)$$

- **Aggregate Proportionality Hypothesis:**
  - $IFR(x)$ is approximately proportional to $m_A(x)$; equivalently
  - $\log IFR(x)$ is approximately parallel to $\log m_A(x)$
  - $RF(x)$ does not depend much on age
    (compared to the dependence of $m_A(x)$ on age)

# Phase 2: The impact of vaccination and new variants

- Data for 2021: much more complex
- Vaccination: oldest ages in December 2020 $\rightarrow$ teenagers in October/November 2021; then boosters
- New variants in the UK: Alpha; Delta; Omicron
  different levels of severity and lethality
- More variation in behaviour than 2020 as rules relaxed
- What have been the impacts at different ages on:
  - Infection rates?
  - Hospital admissions?
  - Deaths?

# Vaccination and antibody status: Ages 18-24 and 65-69




- Older groups: higher vaccine uptake; antibody decline more rapid
- Younger groups: clinically vulnerable vaccinated early + main wave of vaccinations
- All groups: by the middle of 2022, very high % either infected or vaccinated

# Proportionality Hypothesis

Generalise:

$$m_C(i, x, \theta, t) = m_A(i, x) IR(i, x, \theta, t) RF(i, x, \theta, t)$$

New:

- Time, $t$: improved treatments
- $\theta$: relative frailty depends on a number of factors
  - vaccination status (0, 1, 2, booster)
  - which vaccines have been administered
  - duration since vaccination
  - prior infection status
  - newly infected $\Rightarrow$ which variant
- Infection rates also depend on $\theta$:
  - number and timing of vaccinations
  - behaviour

# Phase 2 Development

By subgroup, $i$, and age $x$:

- $\bar{\boldsymbol{\theta}}(i, x, t) =$ proportions in different states for $\theta$ in subgroup $i$, age $x$ at time $t$
- Phase 2: at any given point in time (e.g. mid 2021)
  Aggregate $\bar{\boldsymbol{\theta}}(i, x, t) =$ is highly variable (e.g. old $\rightarrow$ young)
- Problem: Data lacks granularity with respect to $\theta$
- So difficult to check the validity of the proportionality hypothesis

# Phase 3: Endemic Phase, middle of 2022 onwards

- Antibody prevalence $\Rightarrow$ most people either
  - vaccinated
  - have a prior infection (and recovered) (70% to 90%?)
  - both
- epidemiological studies $\Rightarrow$ not much difference in levels of protection, *except for people who are unvaccinated and have not had a prior infection*
- Basic idea concerning relative frailty:

  $$\text{No Vacc+No Prior} \gg \text{Yes V+No P} > \text{No V+Yes P} > \text{Yes V+Yes P}$$

- Key points:
  - Proportion with no vaccines and no prior infection is very small
  - So impact on aggregate *deaths* (e.g. whole age group) is small

# Phase 3: Endemic Phase, middle of 2022 onwards (cont.)

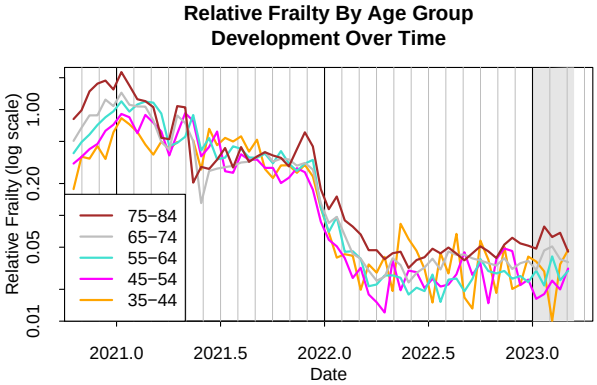
- Data: by national age group only (consistent data through Phases 1, 2, 3)
  - No data to allow estimation of $RF$ by vaccination subgroup etc.
  - No consistent subgroup data (e.g. deprivation) through the three phases

- **Key assumption for Phase 3:**
  - All age groups have approximately the same mix of vaccinations and prior infections
    with negligible differences in RF between vaccinated and previously-infected groups
  - Any variation in $RF(i, \bar{\boldsymbol{\theta}}(i, x, t), t, x)$ due to varying proportions (endemic phase) is much less than intrinsic variation by age
  - Hence: the specifics of each subgroup, $\bar{\boldsymbol{\theta}}(i, x, t)$, do not influence results significantly across age groups

# Assessing the Aggregate Proportionality Hypothesis in Phase 3

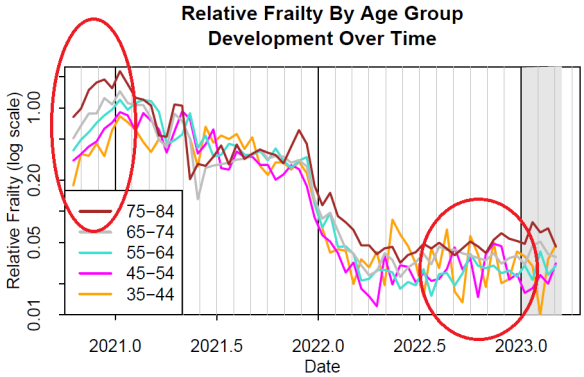
- Data: fortnightly data by age group only (phases 1, 2, 3)
- Infection rates $\rightarrow$ hospitalisations $\rightarrow$ deaths
  $\Rightarrow$ Infection Fatality Rate, $IFR(t, x)$
- Analysis does not differentiate between different vaccination groups
- $RF(t, x) = IFR(t, x)/m_A(x)$
  $m_A(x)$ =pre-covid all-cause mortality excluding external causes
  No differentiation possible between, e.g., vaccination subgroups

# Estimated relatively frailty



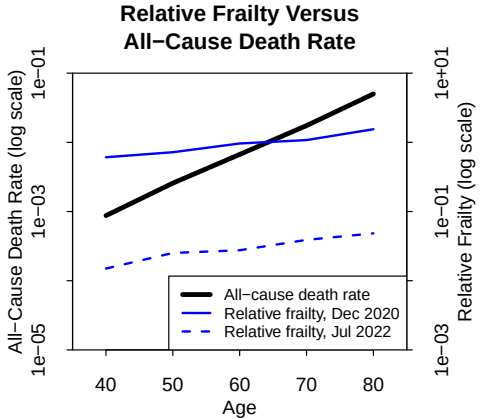

- Covid mortality = all-cause mortality × infection rate × relative frailty
- Steady decline as vaccines take effect; % of prior infections grows; new variants replace older variants

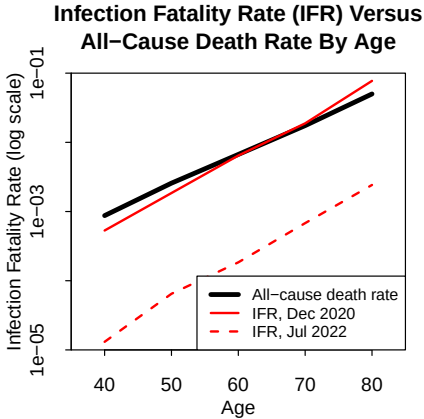
# Estimated relatively frailty: further remarks




- Phase 1 (end of 2020): relative frailty has modest dependence on age
- Phase 2: Vaccination sequencing (old $\rightarrow$ young) causes the age dependency to disappear
- Phase 3: Modest age dependency re-emerges in 2022 after booster roll out to all age groups

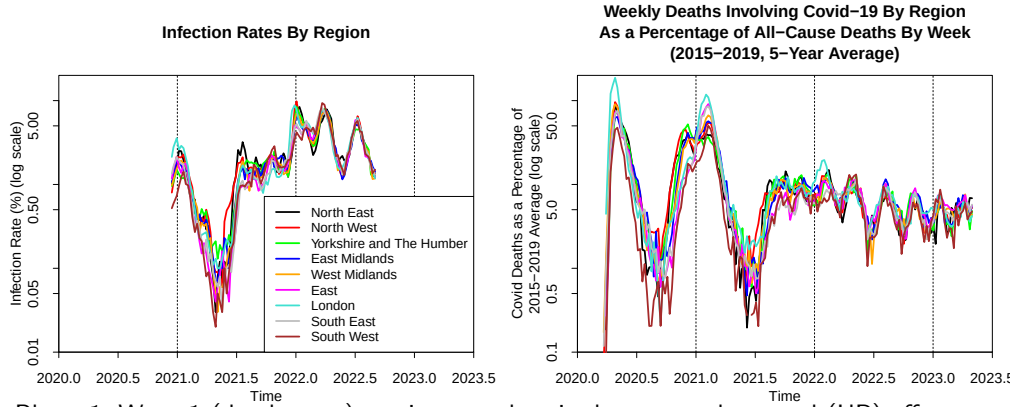
# Aggregate Proportionality Hypothesis: Interpretation




- Left: on a log scale, RF dependence on age much less than all-cause death rate
- Right: on a log scale, IFR is approximately parallel to all-cause death rate
  $\Rightarrow$ on a given date $t$, IFR is approximately proportional to $m_A(x)$

# Infection Rates: Phase 1 to Phase 3



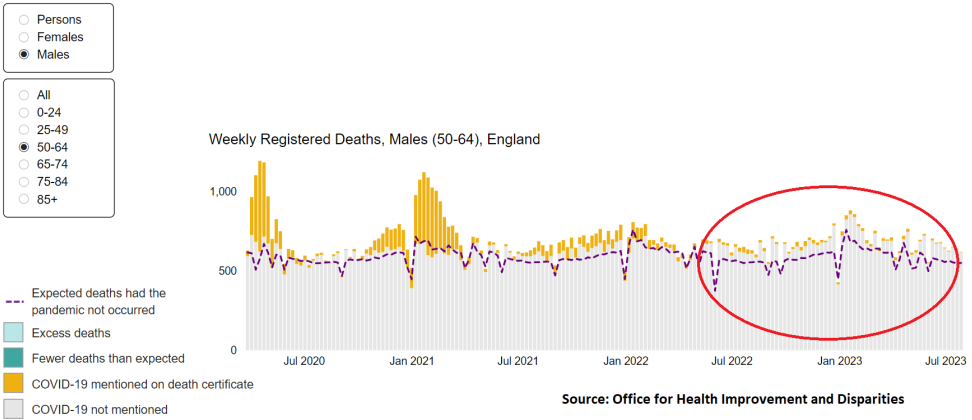

- Phase 1, Wave 1 (death rates): regions synchronised; strong urban-rural (UR) effect
- Phase 1, Wave 2 + Phase 2: regions are not synchronised
- Phase 3: Synchronised waves and much reduced urban-rural effect

# Infection Rates: Phase 1 to Phase 3

Possible interpretations

- Wave 1: Covid already circulating freely around England before March 2020 lockdown
- Wave 2 + Phase 2: restrictions on movement $\Rightarrow$ new waves don't spread easily to other regions
- Phase 3: no restrictions on movement $\Rightarrow$ new variants quickly spread to all regions $\Rightarrow$ return to synchronised
- Diminishing Urban-Rural effect:
  - ??? rural areas benefitted more from lockdown and travel restrictions
  - ??? catchup in rural areas (higher % are susceptible)

# Other insights: Non-Covid Excess Deaths



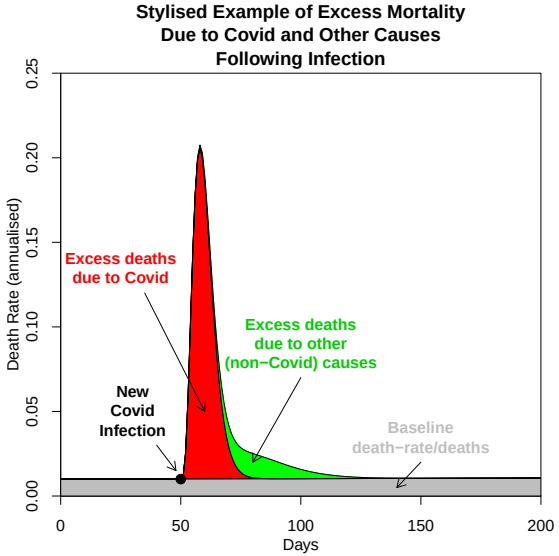

- Expected deaths: projection based on 2015-19 data assuming no pandemic
- Significant excess deaths not attributed to Covid-19
- Possible reasons: optimistic projection; long covid; other

# Other insights: Non-Covid Excess Deaths (cont.)

- Epidemiological studies $\Rightarrow$
  - Covid+Hospital survivors have higher death rates after discharge from hospital than non-Covid people
  - e.g. higher death rates from cardiovascular diseases
  - Reverts to 'standard' mortality over a period of weeks or months
  - 'Long Covid'?? or general *'still not feeling 100%'*
  - Similar pattern to influenza studies
- Other diseases and illnesses will have related patterns
- So each individual, $j$, has a much more volatile death rate $m(j, x)$ compared to their larger subgroup

# Other insights: Non-Covid Excess Deaths (cont.)

Stylised illustration:



# Conclusions

1. Good evidence to support the Proportionality Hypothesis:
   *Covid death rates are approximately proportional to the product of the all-cause death rate and infection rates*
2. But it is complex: *relative frailty* depends on several factors including vaccination status and variant
3. Conclusions should apply to other countries
4. There is a need to understand better excess non-Covid deaths.
   Will they persist into the future linked to endemic Covid-19?

Thank you!

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Paper: available soon – email me!

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