The impact of COVID-19 pandemic on future mortality

International Actuarial Association

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22 November 2022
Potential impact of COVID-19 on mortality

- Ongoing COVID deaths
- Evolution of SARS-CoV-2
- Excess vs COVID
- Post-COVID sequelae
- Impact of delays in diagnosis and treatment
- Emergency healthcare
- Elective healthcare
- mRNA vaccines
Ongoing COVID deaths
Ongoing COVID deaths

UK annual COVID deaths

Protection builds up from boosters and repeated infections; impact of antivirals and other treatments

Less severe variant

More severe variant

Protection wanes / reduces

Created by RGA Global Data & Analytics
Ongoing COVID deaths

Vaccine effectiveness against severe outcomes

Figure 3. The protection against reinfection and hospitalization or severe disease conferred by the primary-series vaccine, first booster vaccine, prior infection, and hybrid immunity compared to immune naive individuals

Source: Bobrovitz et al, Protective effectiveness of prior SARS-CoV-2 infection and hybrid immunity against Omicron infection and severe disease: a systematic review and meta-regression, medRxiv, posted 4 October 2022, available at https://www.medrxiv.org/content/10.1101/2022.10.02.22280610v1 and shared for non-commercial purposes under CC-BY-NC-ND 4.0 (https://creativecommons.org/licenses/by-nc-nd/4.0/)
What if…

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Intermediate
Low Virulence Strong immunity

High virulence Weak immunity

2022?

2021?
Evolution of SARS-CoV-2
Beyond Omicron…

Spike protein: S1 / S2 domains – neutralizing antibodies*

Large antigenic distance – S1 domain
Potential impact of future variants – level of protection is critical

Figure 2. Protection against Omicron conferred by prior infection or hybrid immunity compared to immune naive over time

This analysis uses a log-odds meta-regression model. Points of the same color represent estimates from the same study. The diameter of points varies with the sample size of the study. Dotted lines represent 95% confidence intervals.

Source: Protective effectiveness of prior SARS-CoV-2 infection and hybrid immunity against Omicron infection and severe disease: a systematic review and meta-regression | medRxiv, (preprint 4th October 2022)
Delta’s Enhanced Pathogenicity – Membrane Fusion

Enhanced fusogenicity and pathogenicity of SARS-CoV-2 Delta P681R mutation

Akatsuki Saito, Takashi Irie, ... Kei Sato

Nature 602, 300–306 (2022) | Cite this article

74k Accesses | 104 Citations | 672 Altmetric | Metrics

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Enhanced fusogenicity and pathogenicity of SARS-CoV-2 Delta P681R mutation | Nature (25th November 2021)
Omicron’s Attenuated Pathogenicity - Endocytosis

Attenuated fusogenicity and pathogenicity of SARS-CoV-2 Omicron variant


Nature 603, 700–705 (2022) | Cite this article
23k Accesses | 72 Citations | 469 Altmetric | Metrics

S2 domain – cell entry
N969K substitution

IFR of different variants - log scale

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The routes of SARS-CoV entry into target cells. The viral entry takes... | Download Scientific Diagram (Accessed 14th March 2022)
Ongoing COVID deaths – beyond 2022
Driven by protection against severe outcomes and viral evolution

The altered entry pathway and antigenic distance of the SARS-CoV-2 Omicron variant map to separate domains of spike protein

S1 domain – antigenic distance
S2 domain – determines cell entry
Excess vs COVID
Excess vs COVID in England & Wales

![Chart 2: Comparison of weekly measures of COVID-19 deaths for England & Wales](chart.png)

Relationship between excess and COVID by age

England & Wales

![Chart showing excess and COVID deaths by age in England & Wales in 2021]

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Relationship between excess and COVID by age

United States

US excess (expected based on 2019) vs deaths involving COVID 2021

Ahmad FB, Cisewski JA, Anderson RN. Provisional Mortality Data — United States, 2021. MMWR Morb Mortal Wkly Rep 2022;71:597-600. DOI: http://dx.doi.org/10.15585/mmwr.mm7117e1
Weekly excess deaths split COVID and non-COVID

England & Wales, 2022, Ages 45-64
Weekly excess deaths split COVID and non-COVID

England & Wales, 2022, Ages 65+
### Contributory factors to excess non-COVID deaths in UK

<table>
<thead>
<tr>
<th>Category</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directly related to COVID-19</td>
<td>• Undiagnosed COVID-19</td>
</tr>
<tr>
<td></td>
<td>• Post-COVID-19 sequeliae (hospitalised vs non-hospitalised, new onset vs recurrence):</td>
</tr>
<tr>
<td></td>
<td>• Cardiovascular</td>
</tr>
<tr>
<td></td>
<td>• Neurological</td>
</tr>
<tr>
<td></td>
<td>• Respiratory</td>
</tr>
<tr>
<td></td>
<td>• Diabetes</td>
</tr>
<tr>
<td>Missed healthcare earlier in pandemic</td>
<td>• Missed cancer diagnoses</td>
</tr>
<tr>
<td></td>
<td>• More advanced stage of disease</td>
</tr>
<tr>
<td></td>
<td>• Missed provision of healthcare for other conditions</td>
</tr>
<tr>
<td></td>
<td>• Health issues will have become more serious since then</td>
</tr>
<tr>
<td>Provision of ongoing emergency care</td>
<td>• Ambulance delays</td>
</tr>
<tr>
<td></td>
<td>• A&amp;E waiting times</td>
</tr>
<tr>
<td></td>
<td>• Periods where system is overwhelmed leading to lower quality of care across the board</td>
</tr>
<tr>
<td>Provision of ongoing urgent or routine care</td>
<td>• Health issues will be more serious when eventually presented to healthcare services</td>
</tr>
<tr>
<td></td>
<td>• People still avoiding healthcare system?</td>
</tr>
<tr>
<td></td>
<td>• Reduced GP services</td>
</tr>
<tr>
<td></td>
<td>• Record NHS waiting lists</td>
</tr>
<tr>
<td></td>
<td>• Inadequate staffing levels</td>
</tr>
<tr>
<td></td>
<td>• Inadequate healthcare funding</td>
</tr>
<tr>
<td>Other impacts linked to pandemic / restrictions</td>
<td>• Accelerated deaths / survivorship bias</td>
</tr>
<tr>
<td></td>
<td>• Low seasonal flu / deaths delayed to later in the year</td>
</tr>
<tr>
<td></td>
<td>• Motor vehicle accidents</td>
</tr>
<tr>
<td>Lifestyle and behaviours</td>
<td>• Alcohol-related deaths</td>
</tr>
<tr>
<td></td>
<td>• Suicide</td>
</tr>
<tr>
<td></td>
<td>• Drug overdoses</td>
</tr>
<tr>
<td>Other pandemic-related factors</td>
<td>• Vaccine-related deaths</td>
</tr>
<tr>
<td>Factors not related to pandemic</td>
<td>• Heatwaves</td>
</tr>
<tr>
<td></td>
<td>• Health inequalities</td>
</tr>
</tbody>
</table>
Post-COVID sequelae
Potential impact of COVID-19 on mortality trends

Post-acute impact on survivors of “severe” COVID

Morbidity

- Hospitalised survivors [1]
  - Jan – Aug 2020 + 140 days follow-up
  - Compared to matched controls
  - 3.5x readmission
  - New onset / all events
  - 27x / 6x respiratory disease
  - 5x / 3x major cardiovascular events
  - 3.5x / 1.5x diabetes

Mortality

- Severe COVID-19 vs no COVID-19 [2]
  - Jan – June 2020 + 365 days follow-up
  - 2.50 all-cause hazard ratio controlling for confounders
  - 3.33 for under 65s
  - 2.17 for 65+
  - 80% of deaths not due to respiratory or cardiovascular disease

- Hospitalised survivors [3]
  - Feb. – Dec. 2020 + ≤ 314 days follow-up
  - 4.8x risk of all-cause mortality vs matched controls

Sources:
Potential impact of COVID-19 on mortality trends

Post-acute impact on survivors of COVID

Study - Estonia Health Board

- COVID-19 reportable disease
  - Infected Feb. 2020 – Feb. 2021*
  - Follow-up till Nov 14, 2021

- Severity of COVID infection
  - Non-severe (outpatient): 92%
  - Severe (hospitalization): 5%
  - Critical (ICU): 2%

Mortality

- Infected with COVID vs uninfected
  - One year all cause mortality aHR 3.1
  - 5 week mortality significant
    - Infected COVID 1623 deaths / 10,000
    - Uninfected COVID 118 deaths / 10,000

- Severe / critical 61% of all deaths

- Persistent increased mortality > 60 yrs. age
  - Cardiovascular event aHR 2.1
  - Cancer aHR 1.5
  - Respiratory disease aHR 1.9
  - Other causes death aHR 1.8

Potential impact of COVID-19 on mortality trends

<table>
<thead>
<tr>
<th>Age</th>
<th>Adjusted hazard ratio (95% CI)</th>
<th>p-value</th>
<th>Deaths in SARS-CoV-2 cases/reference group</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 yrs.</td>
<td>4.7 (3.0-7.5)</td>
<td>&lt;0.0001</td>
<td>47/28</td>
</tr>
<tr>
<td>&gt; 60 yrs.</td>
<td>20.1 (15.5-26.1)</td>
<td>&lt;0.0001</td>
<td>402/67</td>
</tr>
<tr>
<td></td>
<td>15.5 (12.1-19.7)</td>
<td>&lt;0.0001</td>
<td>344/80</td>
</tr>
<tr>
<td></td>
<td>7.9 (6.2-9.9)</td>
<td>&lt;0.0001</td>
<td>219/105</td>
</tr>
<tr>
<td>Mid- and long-term</td>
<td>0.9 (0.7-1.2)</td>
<td>0.5360</td>
<td>81/244</td>
</tr>
<tr>
<td>36-50 days</td>
<td>3.9 (2.9-5.1)</td>
<td>&lt;0.0001</td>
<td>104/104</td>
</tr>
<tr>
<td>51-84 days</td>
<td>2.8 (2.2-3.5)</td>
<td>&lt;0.0001</td>
<td>130/184</td>
</tr>
<tr>
<td>85-365 days</td>
<td>1.7 (1.5-1.8)</td>
<td>&lt;0.0001</td>
<td>581/1376</td>
</tr>
</tbody>
</table>

Increased Acute Mortality

Persistent Increased Mortality
Potential impact of COVID-19 on mortality trends

Long COVID – symptoms persisting beyond 12 weeks

- Two major groups:
  - Identifiable pathology – e.g., lung fibrosis (scarring)
  - Non-identifiable pathology – e.g., non-specific fatigue

- More prevalent:
  - Severe illness
    - Anyone who has been infected can experience symptoms
    - Coexisting co-morbidities

- Vaccination may reduce risk ~15%

- Paxlovid reduces post acute risk of death 48%, hospitalization 30%, post-acute sequelae 26%

- Risk appears to vary with variants
  - Odds Long COVID omicron vs. delta of 0.24-0.50 depending on age / time since vaccination

- Wide range of prevalence - multiple reasons why data is unreliable

Potential impact of COVID-19 on mortality trends

Morbidity – Long COVID – 24-month follow-up

**Cohort**

- 1,192 COVID survivors discharged alive
- Confirmed diagnosis + hospitalized
  - 4% in ICU
  - Median age 57
    - 72% middle school or lower
    - 28% college or higher
- % of people with ongoing symptom
  - 68% at 6 months
  - 55% at 24 months*

**Work status**

- 62% retired / jobless / homemaker pre COVID
- 38% Working FT or PT pre-COVID
  - 89% returned to original work at 24 months
  - 11% not returned to original work
    - 4.3% not RTW due to physical function
Impact of missed healthcare during pandemic
Impact on cancer treatment in England

Number of patients starting cancer treatment in England

- Lockdown 1: 23 Mar 2020
- Lockdown 2: 5 Nov 2020
- Lockdown 3: 5 Jan 2021
- Freedom Day: 19 Jul 2021

- c.35k missing cancer treatments
- c.35% fall

Excess mortality by cancer

Source: OHID, available at https://app.powerbi.com/view?r=eyJrIjoiYmUwNmFhMjYtNGZhYS00NDk2LWFiMTA0OTg0OGNHNnFmFiNGM0IiwidCI6ImVlNGUxNDk5LTRhMzUtNGIyZS1hZDQ3LTU5MTQzOTg1NzMiXNAiX09 and available under the Open Government Licence v3.0 (https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/).
Excess mortality by ischaemic heart disease

Source: OHID, available at [https://app.powerbi.com/view?r=eyJrIjoiYmUwNmFhMjYtNGZhYS00NDk2LWFiMTA0OTgGOGNhNmFNGM0iwidCI6ImVlNGUxNDk5LTRhMzUtNGIyZS1hZDQ3LTVmM2NmOWRlODY2NiIsImMiOjF9](https://app.powerbi.com/view?r=eyJrIjoiYmUwNmFhMjYtNGZhYS00NDk2LWFiMTA0OTgGOGNhNmFNGM0iwidCI6ImVlNGUxNDk5LTRhMzUtNGIyZS1hZDQ3LTVmM2NmOWRlODY2NiIsImMiOjF9) and available under the Open Government Licence v3.0 ([https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/](https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/))
c.82k missed ‘heart’ procedures
c.82k missed ‘heart’ procedures: c.10k angioplasty plus stents

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Emergency healthcare
Ambulance response times

Immediate threat to life (eg cardiac arrest)

Serious conditions (eg stroke, chest pain)

Number of beds

Delayed discharges

Average number of people delayed per day / average number of patients no longer meeting criteria to reside, by month in Acute Trusts

A&E emergency admissions

A&E crisis and non-COVID excess deaths

- 4,500 excess deaths due to A&E overcrowding in 2020-21
  - Royal College of Emergency Medicine, November 2021

- May be causing as many as 500 excess deaths per week in recent months
  - John Burn-Murdoch, Financial Times, August 2022
  - [https://twitter.com/jburnmurdoch/status/1562004612172873728](https://twitter.com/jburnmurdoch/status/1562004612172873728)
  - “… a close match for non-COVID excess deaths…”
Mainly COVID excess deaths in hospitals

Source: OHID, available at https://app.powerbi.com/view?r=eyJrIjoiYmUwNmFhMjYtNGZhYS00NDk2LWFiMi1COTg0OGNhNmFNGM0IiwidCI6ImVlNGUxNDk5LTRhMzUtNGIyZS1hZDQ3LTlfY2NlM2M0IiwiaCI6IjgiLCJpcCI6IjEiLCJwIjoiNDA2NDkyNjAhMTk5MDk3Y2E2YjFkNDIwY2ZkOTIyZjIifQ and available under the Open Government Licence v3.0 (https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/)
Non-COVID excess mortality at home

Source: OHID, available at https://app.powerbi.com/view?r=eyJrIjoiYmUwNmFhMjYtNGZhYS00NDk2LWFiMTA0OTg3OGNhNmFNGM0IiwidCI6Iml2Ym9vbF9tZXN0YWdlOmF1dGhvcml0eSBkb2N1bGUITCIsImMiOjZ9
and available under the Open Government Licence v3.0 (https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/)
Deaths by place and age

E&W non-COVID deaths per 1,000 population: All ages, Persons, All causes

Data source: ONS, available under the Open Government Licence
Non-COVID deaths by place and cause, ages 45-64
Non-COVID deaths by place and cause, ages 45-64

E&W non-COVID deaths per 1,000 population: 45 to 64 years, Persons, IX Diseases of the circulatory system

Created by RGA Global Data & Analytics
Data source: ONS, available under the Open Government Licence
Non-COVID deaths by place and cause, ages 45-64

E&W non-COVID deaths per 1,000 population: 45 to 64 years, Persons, X Diseases of the respiratory system

Created by RGA Global Data & Analytics
Data source: ONS, available under the Open Government Licence
Non-COVID deaths by place and cause, ages 45-64
Elective healthcare
NHS England waiting lists

NHS England Referral to Treatment (RTT) waiting times

New joiners to the NHS ‘waiting list’
NHS hospital activity

Hospital activity in England

Created by RGA Global Data & Analytics
Data from NHS Digital, licenced under the current version of the Open Government Licence
Potential impact of COVID-19 on mortality trends

NHS funding

- May 2021: four-year commission of inquiry by LSE and Lancet
  - 4% uplift for next 10 years to 2030-31
  - Meet demand; rebuild after the pandemic; develop resilience against further acute shocks and major threats to health

- Oct 2021: Autumn Budget and Spending Review
  - Resource (day-to-day) spending to rise 3.8% each year in real terms, on average, over 2021-22 to 2024-25; includes £8bn to tackle backlog
  - Also needs to deliver NHS Long Term Plan and continue to tackle COVID

- Oct 2022: Julian Kelley, NHS England CFO, warns there could be up to £7bn shortfall in 2023-24
  - Continuing COVID, NHS staff pay rises, and impact of inflation
  - In addition to £14bn efficiency savings over period to 2024-25
  - Without extra funding services could be cut in cancer, mental health, primary care

- Nov 2022: Autumn statement
  - Tax rises and spending cuts totalling £55 billion
  - But extra £3.3 billion for healthcare spending
  - Independent assessment of NHS workforce needs
Potential impact of COVID-19 on mortality trends

NHS England workforce

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"… the workforce crisis will be the key limiting factor on efforts to boost NHS activity and tackle the rising backlog of care…"

The King’s Fund, 22 Feb 2022
NHS staff absences

Figure 28: 7-day average staff absence of acute and MHLDA (mental health, learning disabilities and autism) trusts. England, from week ending 2 April 2020 to week ending 22 April 2022

mRNA vaccines
mRNA Vaccines in development

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-small Cell Lung Cancer</td>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>Ovarian Cancer</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Brain Cancer</td>
<td>5</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood System Cancer</td>
<td>3</td>
<td>6</td>
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<tr>
<td>Digestive System Cancer</td>
<td>1</td>
<td>2</td>
<td></td>
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<tr>
<td>Rabies</td>
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<tr>
<td>HIV-1 Infection</td>
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<td>1</td>
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<tr>
<td>Zika Virus</td>
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<td>Tuberculosis</td>
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<td>HMPV and HPIVs</td>
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<tr>
<td>Ebola Virus Disease</td>
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<td>Influenza</td>
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<tr>
<td>Respiratory Syncytial Virus</td>
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<tr>
<td>Cytomegalovirus Infection</td>
<td>1</td>
<td>1</td>
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</tr>
</tbody>
</table>

- Many mRNA vaccines were in development before the pandemic
- Focus on COVID vaccine seems to have temporarily slowed development in some cases
- Success of COVID vaccine has naturally led to renewed interest and funding for other vaccines
- Still mostly in Phase 1 or Phase 2 so if successful still several years from approval
  - Phase 1: Typically 12-18 months
  - Phase 2: Typically 2+ years
  - Phase 3: Typically 3-5 years
  - Evaluation and approval: Typically 1-2 years

Summary
Summary: Impact of the pandemic on future mortality

- Ongoing COVID deaths
- Other immediate factors
  - Impact on emergency healthcare
  - Post-COVID sequelae
  - Missed healthcare during the pandemic
- Longer-term factors
  - Missed healthcare during the pandemic
  - Impact on elective healthcare
  - mRNA vaccines
Summary: Impact of the pandemic on future mortality

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Anticipated mortality improvements over 2020-2022?