Excess mortality among people with communicable diseases over a 30-year period, Victoria, Australia: a whole of population cohort study

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Summary

Background Understanding mortality burden associated with communicable diseases is key to informing resource allocation, disease prevention and control efforts, and evaluating public health interventions. We quantified excess mortality among people notified with communicable diseases in Victoria, Australia.

Methods Cases of communicable disease notified in Victoria between 1 January 1991 and 31 December 2021 were linked to the death registry. Informational gain obtained through linkage and 30-day case fatality rates were calculated for each disease. Standardised mortality ratios (SMR) and 95% confidence intervals were calculated up to a year following illness onset.

Findings There were 1,032,619 cases and 5985 (0.58%) died ≤30 days of illness onset. Following linkage, the 30-day case fatality rate increased more than 2-fold. Diseases with high 7-day SMR signifying excess mortality included invasive pneumococcal disease (167.7, 95% CI 153.4–182.7); listeriosis (166.2, 95% CI 121.2–218.3); invasive meningococcal disease (145.9, 95% CI 116.7–178.3); legionellosis (43.3, 95% CI 28.0–62.0); and COVID-19 (21.9, 95% CI 19.7–24.3). Most diseases exhibited a strong negative gradient, with high SMRs in the first 7-days of illness onset that reduced over time.

Interpretation We demonstrated that the rate of death in Victoria's notifiable disease surveillance dataset is underestimated. Further, compared to a general population, there is evidence of elevated all-cause mortality among people notified with communicable diseases often up to one year following illness onset. Not all elevated risk is likely directly attributable to the communicable diseases of interest, rather, it may reflect underlying comorbidities or behaviours in these individuals. Regardless of attribution, infection with communicable diseases may represent a marker of mortality. Key to preventing deaths may be through timely and appropriate transition to primary and preventive healthcare following diagnosis.

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Keywords: Mortality; Communicable diseases; Infectious disease; Public health

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Research in context

Evidence before this study

Estimates of excess mortality are used to assess the direct and indirect effects of major events of public health importance. It is calculated as the difference between the actual number of deaths occurring during a specified period of interest and the number of deaths expected in an equivalent historical period or comparison group. Various methods for quantifying the excess mortality exist and these are typically evaluated for specific events such as seasonal influenza epidemics, extreme weather events or natural disasters, people living with Human Immunodeficiency Virus (HIV), and more recently, the coronavirus disease 2019 (COVID-19) pandemic. We searched Medline from 1 January 1991 to 26 October 2022 for human research studies using the search terms "excess mortality" combined with a list of all communicable diseases notifiable in Victoria, Australia (for a full list of search terms, see Supplementary Material). This yielded 997 articles, of which 416 (41.7%) had a subject heading or keyword of SARS-CoV-2 or COVID-19, 217 (21.8%) of influenza, and 190 (19.1%) of HIV or Acquired Immunodeficiency Disease Syndrome (AIDS) (search results were not mutually exclusive). Remaining studies quantified excess mortality estimates for a range of notifiable communicable diseases (e.g. tuberculosis, hepatitis C, malaria), particular disease groups (e.g. foodborne diseases, vector-borne diseases), co-infections (community acquired pneumonias, viral hepatitis), or among specific populations at risk for which multiple diseases were explored as drivers of excess mortality (e.g. prison populations, occupational cohorts). Due to variations in methods, results are not directly comparable between diseases and studies; however, mortality risks were consistently higher among people with various notifiable diseases compared to background population estimates, including HIV (8-times as high), tuberculosis (6-times), COVID-19 (3-times), *salmonella, campylobacter, yersinia enterocolitica*, and *shigella* infection (3-times), and hepatitis B (1.5-times). Excess all-cause mortality estimates varied for influenza depending on severity of circulating seasonal strains (range, 4.7–52.9-times as high in one study using data from Denmark, Spain and the United States). Whilst many studies used notifiable disease surveillance data to calculate excess mortality estimates, none explored all notifiable diseases concurrently nor did they apply actuarial methods to generate comparator populations specific to the population being studied.

Added value of this study

Our study used population-wide surveillance data linked with death registrations to estimated excess mortality of over 60 communicable diseases notifiable in Victoria, Australia, over a 30-year period. Our unique approach used actuarial methods to calculate standardised mortality ratios: population-derived Life Tables with age- and sex-specific expected mortality rates were used to generate a hypothetical general Victorian population and these rates were compared with mortality rates among people notified with communicable diseases. Mortality ascertainment among those notified with a communicable disease was improved through linkage with the death registry. This method counters some of the limitations of commonly-used methods for estimating mortality burden within populations, including all-cause mortality surveillance, which may overestimate the true number of deaths, and cause-specific mortality analyses, which may underestimate the number. Our findings showed good external validity: For most diseases, excess mortality was particularly pronounced in the first 7-days of illness onset, which reduced as time since illness onset increased. Commonly, death rates returned to expected values by 30-days following illness onset, including for those diagnosed with COVID-19. However, for other diseases, such as those caused by invasive bacterial infections, mortality remained elevated for up to one year following illness onset. We also observed considerable variation in excess mortality by age and disease, with substantially elevated risk of death among younger people and those with invasive bacterial infections such as pneumococcal disease, listeriosis and meningococcal disease.

Implications of all the available evidence

Official statistics relating to disease-specific deaths may undercount the overall contribution they make to all-cause mortality. This study complements other disease-specific excess mortality studies previously published and supports an improved understanding of communicable disease epidemiology, including differential severity of disease. This evidence highlights the value of disease prevention and control measures in reducing mortality risks across populations. The findings also have important implications for clinical practice. Whilst not all excess deaths observed in this, and other studies, are likely to be directly attributable to the communicable diseases of interest, our evidence suggests that infection with communicable diseases may being a marker of individual-level mortality. Key to preventing these deaths may be through the provision of timely and appropriate primary and preventive healthcare following diagnosis or recovery from an acute infection.

Introduction

Understanding the epidemiological characteristics of communicable diseases, including differential mortality, is key to informing allocation of resources, tailoring disease prevention and control efforts, and evaluating public health interventions.[1] Communicable disease surveillance—involving the systematic collection of conditions of public health importance and notifiable by

law—supports the assessment of attributable mortality through the collection of vital status. However, known gaps in surveillance data mean that commonly reported measures of mortality, such as case fatality rates, are often underestimated.[1–3]

Quantifying mortality burden due to communicable diseases from cause-of-death statistics is also challenged by under-ascertainment. Globally, cause-of-death statistics represent the *underlying* cause of death (i.e the disease or injury that initiated the chain of morbid events leading directly to death). These statistics are derived from medical certificates of cause of death (MCCD) completed by medical practitioners. If important contributory causes are not included in the MCCD, nor reflected in underlying cause-of-death statistics, their attribution as a contributing cause may be masked in population-wide statistics, as has been described for several communicable diseases.[4–7] Whilst most deaths in Australia are due to natural causes, a majority have on average 3.2 other diseases or conditions captured on death certificates not reflected in underlying cause-of-death statistics.[8] For example, around a quarter of deaths due to asthma and chronic obstructive pulmonary disease, and 17% of deaths due to dementia, have influenza and pneumonia listed as an associated cause of death. Similarly, 10% of liver cancer deaths have viral hepatitis listed as an associated cause.[8] Compounding this problem is the potential for conditions present at the time of death—which may have contributed to, or hastened, death—being excluded from the MCCD altogether, thus not represented in the underlying or multiple-cause population-wide mortality statistics.

Challenges in communicable disease surveillance and vital registration systems inhibit understanding of communicable diseases mortality burden, limiting the optimal development of public policy. To overcome these challenges, epidemiological methods using all-cause excess mortality statistics are commonly used to provide an objective assessment of the direct and indirect mortality impacts of diseases or major disruptive events. Excess mortality is calculated as the difference between the actual number of deaths occurring during a specified period of interest and the number of deaths expected in an equivalent historical period. It is commonly used to measure the impact of major events of public health importance, including seasonal influenza epidemics,[9] natural disasters,[10] and the COVID-19 pandemic.[11] Excess mortality estimates also provide critical intelligence relating to local capacity for health and other interrelated systems to respond to the health needs of the population. At an individual-level, improved understanding of disease-specific excess mortality may also prompt more focused clinical interventions for those diagnosed with such conditions to preserve life.

Previous research has shown that compared to the general population, risk of death increases following infection with a range of notifiable diseases. For example, mortality in HIV-infected people is consistently higher than among general comparator populations, estimated to be 8.1 times as high in one large Spanish study.[12] Whilst excess mortality may be moderated by early and consistent use of antiretroviral therapy, risk-taking behaviours related to HIV transmission may increase all-cause mortality.[12] Risk of death is also higher for people with tuberculosis, shown to be 6.2-times as high as the general population in the UK.[13] Other chronic conditions such as hepatitis B are also associated with higher risk of death with the all-cause mortality rate exceeding that of the general population by 1.5.[14] Excess all-cause mortality estimates are commonly explored for influenza, which vary markedly by season (ranging from 4.7 to 52.9-times compared to general population estimates).[9] Even relatively mild, self-limiting enteric conditions have been shown to be associated with a 3-times elevated risk of death at one year following infection, including those caused by *salmonella*, *campylobacter*, *yersinia enterocolitica*, and *shigella* species.[15] Excess mortality has commonly been assessed as a measure of the direct and indirect impacts that the COVID-19 pandemic has had on populations around the globe. The estimate varies considerably between and within countries, by time, variant, and by level of COVID-19 vaccination coverage.[16–18] In some geographical areas (e.g. Australia and Denmark)—when aggressive public health and social measures were put in place to limit transmission—the all-cause excess mortality reduced below baseline.[18] One estimate suggests that globally, compared to *reported* COVID-19 mortality rate of 39.2 deaths per 100,000 population, the rate of death is 3-fold higher.[19] Establishing a methods to assess mortality burden by disease and at a local population level is important to support the allocation of finite healthcare resources and to tailor prevention efforts to diseases likely to cause the greatest burden across the population.

There are various statistical approaches to estimating excess mortality, ranging from simple comparisons of observed deaths with historical averages, to the application of generalised linear, trigonometric, stochastic and Bayesian models.[20] These methods may draw on all-cause or cause-specific mortality data obtained from vital registries. Estimation of excess mortality using *all-cause* mortality surveillance (and without linkage to other surveillance sources such as disease registries) may overestimate the true number of deaths associated to a cause of interest. In contrast, estimation of excess mortality using *cause-specific* mortality data (where the condition of interest is listed as the underlying or contributory cause of death on a MCCD) may result in reduced sensitivity and underestimate the true number of deaths.[9] Further, these methods commonly use a general comparator populations as the baseline from which to measure expected number of deaths. This

approach may be limited by differences between general comparator populations and the population of interest, including variations in size and age structure of the populations or changes to societal conditions over time. The calculation of standardised mortality ratio (SMR) accounts for these population dynamics. The use of individual-level probabilities of death—as distinct from population-wide, historical mortality data—supports calculation of expected number of deaths and strengthen the accuracy of excess mortality estimates. The use of population-wide surveillance datasets linked with vital registration systems enables complete ascertainment of vital status,[21] likely increasing the specificity of estimates than those generated by all-cause methods, and supports concurrent examination of all notifiable conditions of public health importance across a whole population, as distinct from disease-specific or small-site observational studies.[21,22]

In Australia, a person's vital status is a mandatory data element for the National Notifiable Disease Surveillance System, to which the State of Victoria contributes. However, for most conditions, vital status is provided at the time of notification and only updated during public health investigations. Such investigations may involve interview with the case or treating clinician at or around the time of notification, and not be reflective of a person's vital status thereafter. We hypothesise that the mortality rate is underestimated among a range of notifiable conditions notified in Victoria, and that the rate of death among people notified with such conditions may be greater than a general comparator population. Here, we augmented surveillance data with vital registration data and applied actuarial methods using expected rate of death at an individual-level to calculate excess mortality among people notified with communicable diseases in Victoria, Australia: the southernmost mainland state of Australia with a population of 6.5 million.

Methods

Data sources

The study used linked records from three population-wide datasets in Victoria, Australia. The primary cohort was all confirmed and probable cases of communicable disease notified to the Victorian Department of Health with an illness onset of between 1 January 1991 and 31 December 2021. In Victoria, more than 80 conditions are required to be notified by medical practitioners and laboratories under the Public Health and Wellbeing Act (2008).[23] Certain notifiable conditions were excluded from this study, including cases of anaphylaxis and sexually transmissible infections. The full list of excluded conditions is provided in the Supplementary file. The primary cohort were sourced from two surveillance systems: Public Health Event Surveillance System (PHESS) and Transmission and Response Epidemiology Victoria (TREVi). PHESS captures all notifiable conditions excluding COVID-19, which is captured on TREVi. Both datasets contain socio-demographic and limited clinical data relating to the case, including age, sex, date of illness onset, and causative pathogen. Vital status is also captured, usually completed at time of notification or during public health investigations.

The primary cohort was linked to the Victorian Death Index (VDI) to identify deaths occurring among these individuals between 1991 and 2021. VDI contains all registrable deaths occurring in Victoria under the Births, Deaths and Marriages Registration Act 1996,[24] and includes identifying information about the deceased, causes of death and date of death. Record linkages were carried out by the Centre for Victorian Data Linkages at the Victorian Government Department of Health (Supplementary file). To assess potential biases in linkage success, we summarised socio-demographic characteristics of deceased cases, disaggregated by presence of an all-cause linked death record.

Expected mortality rates *(qx)*—representing the probability of death over one year, by single age, sex and calendar year (1991–2020)—were sourced from life tables compiled by the Australian Bureau of Statistics (ABS),[25] with *qx* values from 2020 applied to 2021, in the absence of more contemporaneous data.

Data preparation

A new binary variable representing each case's vital status was created using the information from the original disease notification record (as captured PHESS or TREVi), and enhanced with information contained within the VDI record, if present. Specimen collection date of the first positive specimen, or date of notification to the Department of Health, were used as proxies for date of illness onset if onset date was unknown or for those with asymptomatic infection. Deceased cases were grouped into the following categories, reflecting time of death relative to illness onset: 0–<7 days; 7–<30 days; 30–<90 days; 90–≤365 days.

We applied the mortality rate (*qx*) to each individual in our primary cohort, which was used in the statistical analyses to generate a hypothetical comparator population. Cases with missing data relating to age and sex were excluded, and thus the cohort was considered a *complete-case analysis*. Missing data was non-differential by the outcome of interest—excluded from both the numerator (observed values) and denominator (expected values) of our SMR calculations—thus eliminating any bias caused by missing data. Descriptive statistics exploring characteristics of the excluded cohort are provided in Tables S1–S4 of the Supplementary file.

Statistical analysis

Informational gain through linkage was assessed for each condition by comparing crude 30-day case fatality

rate (CFR) prior to and after linkage. CFR was calculated using the number of all-cause deaths occurring <30 days of illness as the numerator, and the total number of reported cases for each condition as the denominator, with the rate expressed as per 10,000 cases.

We applied actuarial methods using expected rate of death (*qx*) at an individual-level to calculate excess mortality. Excess mortality was assessed by calculating standardised mortality ratios (SMR) for each condition using the formula: $SMR = \frac{O}{E}$, where O represents the observed numbers of deaths during the follow-up period of interested (using the enhanced vital status); and E represents expected deaths estimated by the sum of the age-, sex, and year-specific probability of death (*qx*) for each case. Ninety-five percent confidence intervals were calculated using Vandenbroucke Method.[26] SMR >1 represents exceedant rate of death in the cohort of interest over and above that of the expected comparator population. SMRs were stratified by broad age-groups: 0–14 years, 15–64 years, and ≥65 years.

Approvals

Study approvals were obtained from the Victorian Government Department of Health Research Ethics Committee (reference: LNR/47982), and registered with Monash University Human Research Ethics Committee (reference: 30076).

Role of the funding source

No funding was provided for this study.

Results

There were 1,032,619 notified cases during the study period. Of these, 4492 (0.44%) were reported as being deceased, with 2886 (0.28%) occurring ≤30 days of illness onset. After linkage with VDI, 72,551 (7.05%) cases had a corresponding all-cause death record, unbounded by time since illness onset. When this was restricted by time, 18,075 (1.75%) deaths occurred ≤365 days of their notifiable disease illness onset date and 5985 (0.58%) occurred ≤30 days, the latter representing a more than 2-fold information gain obtained through linkage compared to unlinked data alone (CFR = 28 per 10,000 cases vs 58 per 10,000 cases). Socio-demographic characteristics of the cohort are shown in Table 1, with proportionally fewer deaths among younger people, females and those living in inner metropolitan areas of Victoria. Proportionally fewer female, Aboriginal and/or Torres Strait Islander, and non-Australian born cases had a linked VDI record, likely signalling challenges in linkage success due to, for example, changes in family names and/or other identifying data (Table S4, Supplementary file).

Condition-specific case fatality rates

For most conditions, the 30-day CFRs increased following linkage with VDI. Information gain obtained through linkage was notable for varicella zoster virus (CFR = 0.3 vs 50.7 per 10,000 cases), campylobacter infection (0.7 vs 17.3 per 10,000 cases), hepatitis B (1.2 vs 16.4 per 10,000 population) and pertussis (0.8 vs 7.2 per 10,000 cases) (Table 2).

Condition-specific excess mortality

Conditions with the highest 7-day SMR (total, all ages) signalling excess mortality were: Creutzfeldt-Jakob disease (425.6, 95% confidence interval [CI], 269.4–617.3); invasive pneumococcal disease (167.7, 95% CI 153.4–182.7); listeriosis (166.2, 95% CI 121.2–218.3); invasive meningococcal disease (145.9, 95% CI 116.7–178.3); *legionella pneumophila* infection (43.3, 95% CI 28.0–62.0), COVID-19 (21.9, 95% CI 19.7–24.3), hepatitis A (19.6, 95% CI 5.0–42.9), influenza (14.9, 95% CI 13.7–16.2), salmonellosis (12.1, 95% CI 9.5–15.0), and tuberculosis (10.1, 95% CI 6.9–13.9). (Fig. 1a–e and Table S5, Supplementary file).

Most conditions exhibited a strong, negative gradient: highest SMRs were typically observed in the first 7-days of illness onset, gradually declining over time. Excess mortality for some conditions remained elevated to one year following illness onset, whilst for others, SMR returned to baseline or below (where SMR ≤1) by 30 or 90 days (Fig. 2). Invasive pneumococcal disease, for example, showed a negative gradient of excess mortality over time, with excess mortality highest <7 days of illness onset, but remaining significantly elevated across all time points and up to one year following illness onset (Fig. 1a). In contrast, excess mortality for invasive meningococcal disease was substantially elevated up to 30 days, returning to baseline thereafter (Fig. 1a). Mortality also returned to baseline for COVID-19, hepatitis A and *Legionella longbeachae* infection at between 90 and <365 days following illness onset (Fig. 1a, b, d).

There was significant variation in excess mortality by age, with markedly higher SMRs in younger age-groups, reflecting a reduced probability of death in younger people generally. Among those aged 0–14 years, and for conditions with >5 deaths occurring within 7-day of illness onset, 7-day SMR was highest for invasive meningococcal disease (1193.9, 95% CI 779.1–1696.9), invasive pneumococcal disease (674.6, 95% CI 436.1–964.9) and influenza (62.7, 95% CI 36.5–96.1) (Fig. 1a). Substantially more absolute deaths occurred in people aged 15–<64 years. Among conditions with an annual incidence of >5 cases per 100,000 population, elevated 7-day SMRs were observed for listeriosis (1360.2, 95% CI 759.0–2135.7), invasive pneumococcal disease (856.2, 95% CI 725.1–998.2) and *legionella pneumophila infection* (76.3, 95% CI 27.5–149.6).

Variation in excess mortality was also observed across invasive pneumococcal serotypes, with high absolute and excess mortality among people infected with *Streptococcus pneumonia* type 3 (7-day SMR 223.1, 95%

	Total	Alive	Deceased
	N = 1,032,619	N = 960,068	N = 72,551
10-year age group			
0–9	150,403 (14.6%)	149,885 (15.6%)	518 (0.7%)
10–19	106,722 (10.3%)	105,840 (11.0%)	882 (1.2%)
20–29	171,065 (16.6%)	168,188 (17.5%)	2877 (4.0%)
30–39	158,492 (15.3%)	154,524 (16.1%)	3968 (5.5%)
40–49	126,114 (12.2%)	121,130 (12.6%)	4984 (6.9%)
50–59	109,422 (10.6%)	102,405 (10.7%)	7017 (9.7%)
60–69	92,476 (9.0%)	82,110 (8.6%)	10,366 (14.3%)
70–79	62,042 (6.0%)	47,385 (4.9%)	14,657 (20.2%)
80+	55,883 (5.4%)	28,601 (3.0%)	27,282 (37.6%)
Sex			
Female	511,502 (49.5%)	477,669 (49.8%)	33,833 (46.6%)
Male	521,117 (50.5%)	482,399 (50.2%)	38,718 (53.4%)
Aboriginal and Torres Strait Islander origin			
Aboriginal	14,555 (1.4%)	13,648 (1.4%)	907 (1.3%)
Torres Strait Islander	782 (0.1%)	748 (0.1%)	34 (0.0%)
Both	1498 (0.1%)	1387 (0.1%)	111 (0.2%)
Not Aboriginal nor Torres Strait Islander	708,292 (68.6%)	638,348 (66.5%)	69,944 (96.4%)
Question unable to be asked	307,018 (29.7%)	305,463 (31.8%)	1555 (2.1%)
Patient refused to answer	474 (0.0%)	474 (0.0%)	0 (0.0%)
Born in Australia			
No	197,776 (19.2%)	172,994 (18.0%)	24,782 (34.2%)
Yes	474,855 (46.0%)	427,452 (44.5%)	47,403 (65.3%)
Missing	359,988 (34.9%)	359,622 (37.5%)	366 (0.5%)
Remoteness			
Major Cities of Australia	826,401 (80.0%)	771,944 (80.4%)	54,457 (75.1%)
Inner Regional Australia	164,648 (15.9%)	150,132 (15.6%)	14,516 (20.0%)
Outer Regional Australia	30,098 (2.9%)	26,695 (2.8%)	3403 (4.7%)
Remote Australia	408 (0.0%)	378 (0.0%)	30 (0.0%)
Very Remote Australia	20 (0.0%)	19 (0.0%)	1 (0.0%)
Missing	11,044 (1.1%)	10,900 (1.1%)	144 (0.2%)

[a]Vital status enhanced through linkage includes any person notified with a communicable disease over the 30-year study period with a linked death record, unbounded by time.

Table 1: **Characteristics of cohort (Victorian communicable disease surveillance data, 1991–2021), by vital status enhanced through linkage.[a]**

CI 173.5–278.8) and type 19 F (7-day SMR, 428.3, 95% CI 315.7–558.0) (Supplementary file).

Discussion

Using linked surveillance and administrative data, we demonstrated that all-cause mortality is often greater among people notified with a range of communicable diseases up to a year following illness onset than when compared to the expected mortality rate in the general population. For most conditions, a negative gradient was observed with excess mortality most pronounced in the first 7-days of illness onset, reducing as time since illness onset increased. There was considerable variation in excess mortality by age and condition, with substantially elevated risk of death among younger people and those with invasive bacterial infections. These findings support an improved understanding of the differential mortality of communicable diseases and highlights the value of disease prevention and control efforts, including prevention of initial infection, as well as timely and appropriate transition to primary and preventive healthcare following diagnosis.

Of the 63 notifiable conditions analysed, there were several notable findings. We found, that among notifiable bacterial infections, invasive pneumococcal disease caused by *Streptococcus pneumoniae* was associated with the highest absolute and relative number of deaths at 7-days following illness onset. Overall mortality for people with invasive pneumococcal disease is reported to be high.[27] Several pneumococcal serotypes are preventable by vaccination, and our analyses of excess mortality by serotype revealed considerable variation between serotypes, with highest mortality risks linked to serotypes 3 and 19 F. Both serotypes are included in the 23-valent adult and 13-valent paediatric

Condition	Number of deaths ≤30 days of illness onset		Total cases	30-day case fatality rate per 10,000		Percent change[a]
	Pre-linkage (original)	Post-linkage (enhanced)		Pre-linkage (original)	Post-linkage (enhanced)	
Anthrax	<5	<5	<5	0.0	0.0	nc
Arbovirus infection	<5	<5	103	0.0	0.0	nc
Barmah forest virus infection	<5	<5	780	0.0	0.0	nc
Botulism	<5	<5	8	0.0	0.0	nc
Brucellosis	<5	<5	47	425.5	638.3	50.0
COVID-19	1467	1481	213,804	68.6	69.3	1.0
Campylobacter infection	11	272	156,833	0.7	17.3	2372.7
Chikungunya virus infection	<5	<5	279	0.0	0.0	nc
Cholera	<5	<5	15	0.0	0.0	nc
Creutzfeldt-Jakob disease	71	75	188	3776.6	3989.4	5.6
Cryptosporidiosis	<5	12	13,553	1.5	8.9	500.0
Dengue	<5	<5	3175	3.1	3.1	0.0
Diphtheria	<5	<5	<5	0.0	0.0	nc
Zika virus infection	<5	<5	21	0.0	0.0	nc
Food- or water-borne infection, viral	29	382	16,460	17.6	232.1	1217.2
Food- or water-borne infection, bacterial	<5	7	398	0.0	175.9	nc
Food- or water-borne infection, other	8	47	5675	14.1	82.8	487.5
Haemolytic Uraemic syndrome	<5	<5	83	241.0	481.9	100.0
Haemophilus influenzae B	<5	<5	264	75.8	151.5	100.0
Hepatitis A	6	11	3287	18.3	33.5	83.3
Hepatitis B–newly acquired	<5	<5	2440	4.1	16.4	300.0
Hepatitis B–unspecified	6	84	51,246	1.2	16.4	1300.0
Hepatitis C–newly acquired	<5	<5	2962	0.0	0.0	nc
Hepatitis C–unspecified	24	204	79,904	3.0	25.5	750.0
Hepatitis D	<5	<5	267	37.5	112.4	200.0
Hepatitis E	<5	<5	203	0.0	49.3	nc
Hepatitis–virus unspecified	<5	<5	13	0.0	0.0	nc
Influenza	282	1497	202,701	13.9	73.9	430.9
Japanese encephalitis	<5	<5	<5	0.0	0.0	nc
Kunjin virus infection	<5	<5	5	0.0	0.0	nc
Legionellosis, other	16	20	179	893.9	1117.3	25.0
Legionella longbeachae infection	20	24	411	486.6	583.9	20.0
Legionella pneumophila infection	43	69	1760	244.3	392.0	60.5
Leprosy	<5	<5	45	0.0	0.0	nc
Leptospirosis	<5	<5	403	0.0	0.0	nc
Listeriosis	54	89	522	1034.5	1705.0	64.8
Malaria	<5	<5	2563	0.0	7.8	nc
Measles	<5	<5	1296	0.0	0.0	nc
Invasive meningococcal disease	63	95	2059	306.0	461.4	50.8
Mumps	<5	<5	709	0.0	0.0	nc
Mycobacterium ulcerans	<5	<5	2324	0.0	8.6	nc
Paratyphoid	<5	<5	479	0.0	0.0	nc
Pertussis	5	44	61,095	0.8	7.2	780.0
Invasive pneumococcal disease	611	797	8187	746.3	973.5	30.4
Poliomyelitis	<5	<5	<5	0.0	0.0	nc
Psittacosis	<5	8	1270	23.6	63.0	166.7
Q Fever	<5	<5	1039	0.0	9.6	nc
Rabies	<5	<5	<5	0.0	10000.0	nc
Ross river virus infection	<5	<5	8791	0.0	0.0	nc
Rotavirus	<5	<5	1147	0.0	26.2	nc
Rubella	<5	<5	4374	0.0	0.0	nc
Salmonellosis	29	169	52,954	5.5	31.9	482.8
Salmonella enteritidis	8	9	3063	26.1	29.4	12.5
SARS, excluding COVID-19	<5	<5	<5	0.0	0.0	nc

(Table 2 continues on next page)

Condition	Number of deaths ≤30 days of illness onset		Total cases	30-day case fatality rate per 10,000		Percent change[a]
	Pre-linkage (original)	Post-linkage (enhanced)		Pre-linkage (original)	Post-linkage (enhanced)	
(Continued from previous page)						
Shiga-toxin, Vero-toxin producing *E. coli*	<5	8	632	31.6	126.6	300.0
Shigellosis	<5	<5	5416	0.0	1.8	nc
Tetanus	<5	<5	22	0.0	454.5	nc
Tuberculosis	110	120	10,576	104.0	113.5	9.1
Nontuberculous mycobacteria spp	<5	18	1107	9.0	162.6	1700.0
Typhoid	<5	<5	737	0.0	0.0	nc
Varicella zoster infection (Chickenpox)	<5	6	11,722	0.9	5.1	500.0
Varicella zoster infection (Shingles)	<5	51	22,934	1.3	22.2	1600.0
Varicella zoster infection (Unspecified)	<5	355	70,075	0.3	50.7	17,650.0

Pre-link (original) column denotes number of deaths captured on notifiable disease surveillance datasets only and prior to enhancement through linkage with the Victorian Death Index; Post-link (enhanced) column denotes number of deaths captured on notifiable disease surveillance datasets and enhanced through linkage with the Victorian Death Index; Case fatality rates are calculated per 10,000 cases. NEC, Not elsewhere classified; nc, not calculable; COVID-19, Coronavirus diseases 2019; SARS, Severe acute respiratory syndrome. [a]Percent change represents proportion of information gain achieved through linkage with the Victorian Death Index (post-link vs pre-linked case fatality rates).

***Table 2*: Number of deaths occurring within 30 days of illness onset and case fatality rates pre and post linkage with the Victorian Death Index, by notifiable conditions, Victorian communicable disease surveillance data, 1991–2021.**

vaccine formulations under Australia's National Immunisation Program, however a high number of vaccine failures are known to be associated with these serotypes.[28] Despite moderate-to-good vaccine effectiveness against serotype 3 and 19 A from both the paediatric[29,30] and adults[31,32] formulations, differential mortality burden is notable, requiring improvements to existing vaccines. Improved 20- and 15-valent vaccines were recently recommended for clinical use in adults in the United States[33] and these are currently being considered for use in Australia.[34] Monitoring differential mortality by serotype thus supports vaccine development and ongoing surveillance relating to vaccine effectiveness across local population. Infection with *Listeria monocytogenes* was also associated with markedly elevated risk of death. Whilst there is no vaccine available to support prevention efforts, improved awareness of the risk of death following infection can help clinicians provide both focused and enduring care over the short- and long-term following diagnosis.

Morbidity and mortality risks of infectious diseases are known to persist beyond the acute phase of infection. Commonly, these risks are the consequence of cardiovascular damage precipitated by infection and the related inflammatory response. This has been documented for community acquired pneumonias including pneumococcal disease,[35,36] sepsis,[37] influenza, and COVID-19.[38] Consistent with previous studies, our results demonstrated that for many conditions, mortality risks remained significantly elevated even after 30-days following illness onset. This was notable for invasive bacterial infections such as pneumococcal disease, which was non-differential by age, with excess mortality persisting up to 365-days following illness onset in children as it did in older people. Enteric pathogens such as listeriosis, salmonellosis and campylobacter infection also remained elevated to 365-days following illness onset in adolescents and adults, consistent with other studies.[15] The evidence of a persistent risk of death up to one year following illness onset provides a signal to treating practitioners for the need for enduring and wholistic care to patients diagnosed with these and other notifiable conditions examined in our study.

Viral infections such as COVID-19 showed substantially elevated risks of mortality in the first 30-days following illness onset, reducing to baseline by between 90 and <365-days after illness onset. Influenza showed a similar gradient, although excess mortality remained significantly elevated beyond 90-days. This is likely reflective of differences in the characteristics of people commonly tested for influenza, including older people with significant comorbidities who may be at-risk of severe outcomes of influenza disease. This contrasts with the characteristics of people tested for COVID-19, which during Victoria's COVID-19 pandemic response, was indiscriminate by age and presence of pre-existing risk factors. These findings provide reassurance to patients and clinicians that risk of death following infection with diseases such as COVID-19 and influenza is somewhat finite, thus minimising need for prolonged monitoring and active clinical care.

Using age-, sex- and year-specific probabilities of death, we observed persistence of excess mortality at an individual-level over time. This contrasts with traditional methods of calculating excess mortality using population-wide comparators. We observed variation in risk of death by age. However, results should be interpreted with caution as other person-level factors may be driving or contributing to the mortality rates observed.

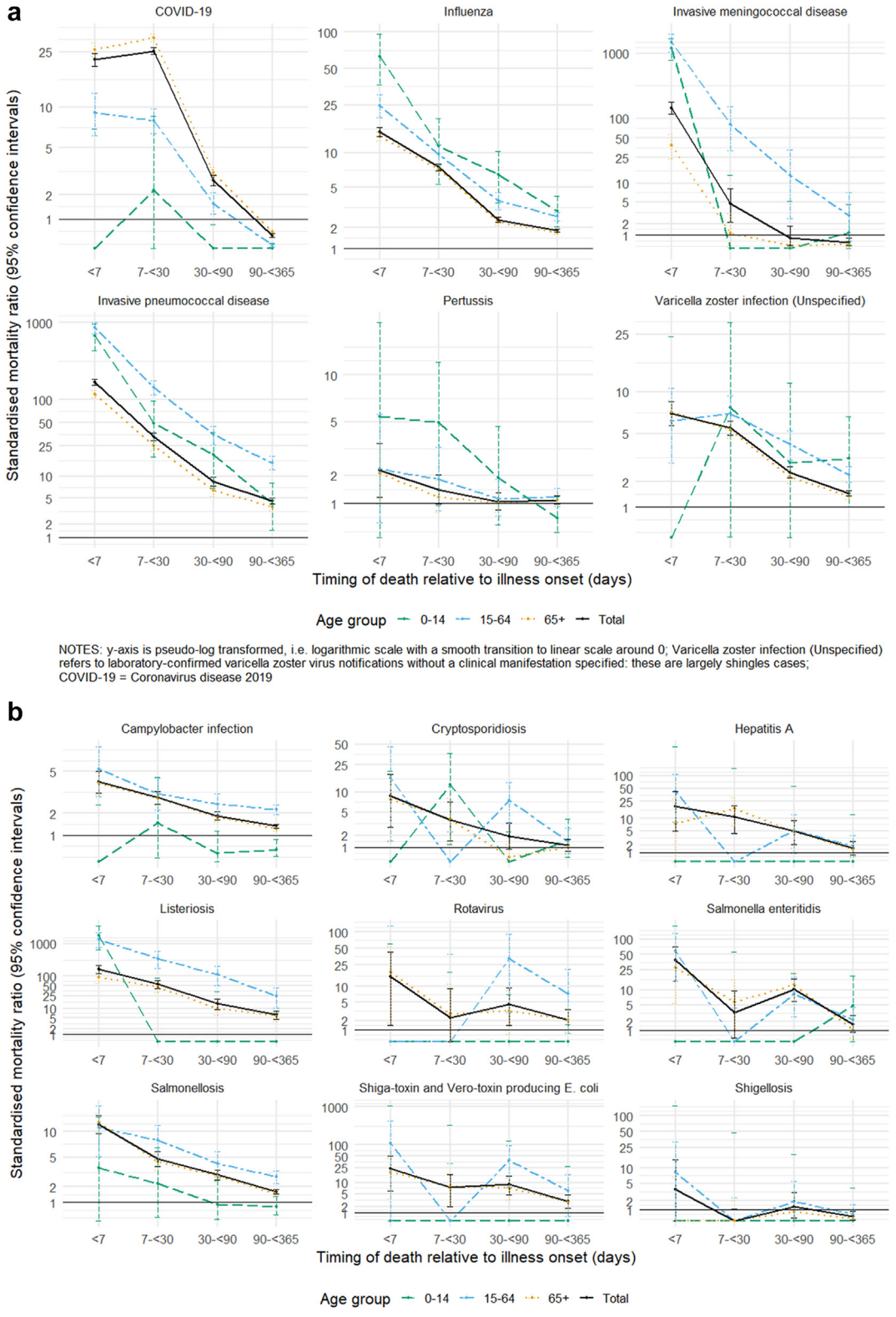
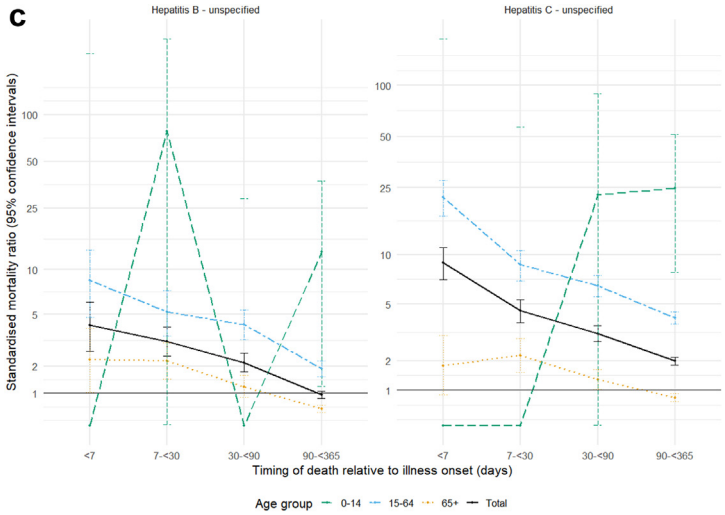
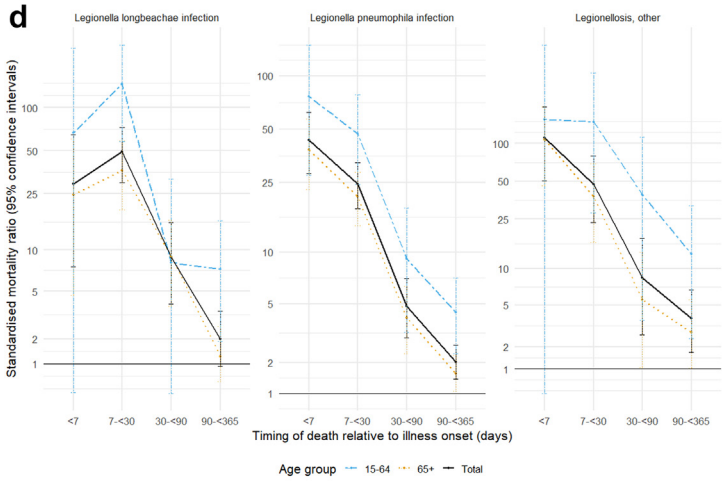


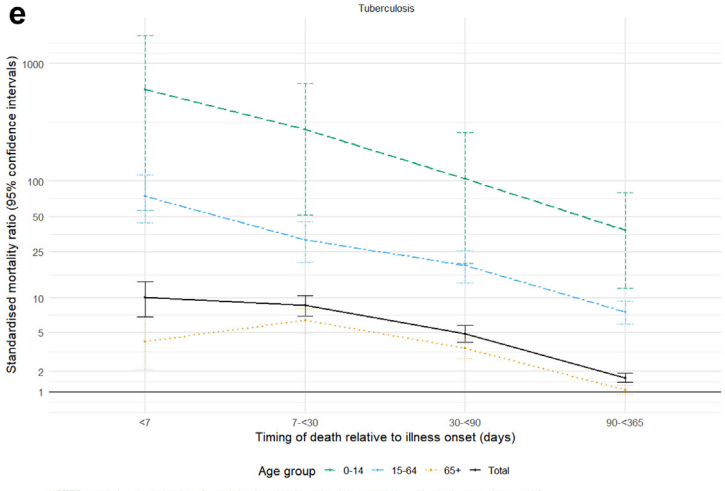
Fig. 1: **a: Standardised mortality ratio, by time since illness onset, by selected vaccine preventable diseases. b: Standardised mortality ratio, by time since illness onset, by selected enteric diseases. c: Standardised mortality ratio, by time since illness onset, by selected bloodborne virus diseases. d: Standardised mortality ratio, by time since illness onset, by selected *legionella* species. e: Standardised mortality ratio, by time since illness onset, by Tuberculosis.**



NOTES: y-axis is pseudo-log transformed, i.e. logarithmic scale with a smooth transition to linear scale around 0; In Australia, Hepatitis B and Hepatitis C notifications are classified according to the timing that the infection was acquired relative to diagnosis. Unspecified notifications are those without evidence that the infection was acquired in the 24 months prior to diagnosis, and represent a majority of all Hepatitis B and C notifications.



NOTES: y-axis is pseudo-log transformed, i.e. logarithmic scale with a smooth transition to linear scale around 0; Nil cases observed among 0-14 year age group



NOTES: y-axis is pseudo-log transformed, i.e. logarithmic scale with a smooth transition to linear scale around 0.

Fig. 1: Continued.

	Condition	7-day SMR	Risk over time	Risk by age group
Bacterial infections	Invasive pneumococcal disease	168	↘ to 365-days	
	Listeriosis	166	↘ to 365-days	
	Invasive meningococcal disease	146	↘ to 30-days	
	Legionella pneumophila infection	43	↘ to 365-days	
	Legionella longbeachae infection	29	↘ to 90-days	
	Salmonellosis	12	↘ to 365-days	
	Campylobacter infection	4	↘ to 365-days	
	Tuberculosis	10	↘ to 365-days	
Viral infections	COVID-19	22	↘ to 90-days	
	Hepatitis A	19	↘ to 90-days	
	Hepatitis C	9	↘ to 365-days	
	Influenza	16	↘ to 365-days	
	Shingles	1	⇝ variable	

Notes: SMR, Standardised mortality ratio; 7-day SMR shown is for all ages aggregated (total); ↘ downward arrow indicates negative gradient of excess mortality, with highest SMR occurring 0-<7 days following illness onset and declining as time since illness onset increases. ⇝ Squiggly arrow indicates no clear gradient of excess mortality over time. Time in days represents period of time following illness onset elevated mortality was observed, e.g. we observed an elevated risk of mortality up to 365-days following illness onset among people notified with Listeriosis; in contrast, elevated risk of mortality remained only up to 30-days following illness onset among people notified with invasive meningococcal disease. Ages 0 to <15 years; 15 to <65 years 65+ years.

Fig. 2: **Selected condition-specific excess mortality, 7-day Standardised Mortality Ratio (SMR), gradient over time and age groups at risk of elevated mortality.**

The excess mortality demonstrated in our study by age and time may represent underlying comorbidities present in people notified with communicable diseases, as distinct from a direct association with their infection alone. For example, excess mortality was observed up to a year following illness onset among people aged >65 years with legionellosis. However, patient-level risk factors for legionellosis include smoking and underlying illnesses such as diabetes, renal failure, chronic lung disease, or other immunocompromising conditions.[39] As such, the extent to which excess mortality demonstrated in this study is due to infection with *Legionella* species or underlying comorbid risk factors remains unclear. Similarly, persistent excess mortality among listeriosis cases may be attributable to underlying comorbidities rather than infection alone. Excess mortality observed in other conditions—such as hepatitis C—may be attributable to behavioural factors that elevate a person's risk of death such as injecting drug use.[40] Further, the excess mortality observed—particularly for conditions such as legionellosis, listeriosis, shingles and influenza—is likely reflective of both underlying frailty as well as an early signal of elevated mortality due to the notifiable disease of interest. The presence of these conditions in frail or immunocompromised individuals may therefore represent a *marker* of mortality risk, prompting a need for more focused clinical and public health interventions tailored to these groups. For example, immunocompromised patients with a recent listeriosis infection requiring hospitalisation should be transitioned to primary care that supports consideration of their overall comorbid profile in the context of recovery from a major infection. Similarly, a newly diagnosed hepatitis C infection may indicate the presence of risk-taking behaviours such injecting drug use. Re-engaging these patients into care and ensuring access to drug prevention services and antiviral treatment services – as routinely occurs in the UK[41]—may minimise risk of death.

The use of population-wide surveillance and administrative datasets provided a robust platform to address our research question, thus not limited by small or convenience samples. Further, ascertainment of the main outcome of interest (death) was very good, in

contrast to other studies that may be impacted by under-reporting of deaths in vital registration systems.[1,42] The inclusion of all communicable diseases of public health importance enabled comparison between conditions, supporting an improved understanding of the relative mortality burden across conditions, and helping to focus public health and clinical action to support prevention efforts. This study highlighted the utility of record linkage to improve mortality ascertainment in communicable disease surveillance datasets, enabling a more accurate assessment of mortality burden. Other national and international jurisdictions could adopt a similar approach to support communicable disease surveillance.

Some limitations of our study are recognised. First, we used all-cause mortality, reducing our ability to ascertain whether deaths were attributable to the notifiable condition of interest or other factors. Some of the excess mortality observed in our study may reflect underlying comorbidities or other risk factors for disease. Nonetheless, our use of communicable disease notifications linked to vital registry data enabled the generation of excess mortality estimates that are likely be more specific than other *all-cause* methods and more sensitive than *cause-specific* methods. Validation studies would be helpful to quantify this. Second, we were unable to explore seasonal factors nor secular trends using this method. Third, our linkage methodology used a deterministic approach, requiring exact matches of identifying data between the linked dataset, which may have increased our type 2 error rate. Our results showed proportionally more records were successfully linked among men than women, and Australian-born Victorians than those born overseas. This implies mortality ascertainment may have been differential by these factors. Fourth, as the study relied on historical surveillance and vital registry data, there were limited covariates available for analysis. Further research is needed to verify these results against coded causes of deaths, and to better understand other factors attributable to the observed excess mortality.

We quantified excess mortality burden among people notified with communicable diseases over a 30-year period in Victoria, Australia. For most conditions, mortality was particularly elevated in the first 30-days following illness onset and returned to baseline thereafter (e.g. COVID-19). However, for others such as invasive bacterial infections, mortality remained elevated for up to a year following illness onset. We also explored excess mortality burden by age, providing important quantitative information for clinicians and public health practitioners about age-specific mortality risk. Such intelligence may support more targeted interventions for people being diagnosed with communicable diseases and to mitigate risk of death. Not all excess mortality observed in our study was likely directly attributable to the communicable diseases of interest, rather, it may reflect underlying comorbidities or behaviours in these individuals. Key to preventing deaths in these individuals may be through the provision of timely and appropriate primary and preventive healthcare following diagnosis or recovery from the acute infection.

Contributors

SR and AC conceptualised the study, developed the methodology, had direct access and verified the underlying data reported in the manuscript. SR led project administration, conducted the formal analysis, drafted the original draft of the manuscript, and finalised the manuscript. KL, NS, BC supervised the study conduct and contributed to writing, reviewing and editing the manuscript. JL, LS, and DW supported project administration, data curation, software management and coding. AC supervised the study design, analyses and preparation of the manuscript; and critically reviewed the results of all analyses. All authors contributed to the intellectual content of the manuscript, approved the final manuscript as submitted and agree to be accountable for all components of the work. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Data sharing statement

The data underlying this article are available in the article and in its online supplementary material.

Declaration of interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

TN has clinical trial contracts that provide institutional (not personal) payments to the Murdoch Childrens Research Institute and the University of Melbourne outside submitted work relating to sponsored vaccine trials of several different vaccines by Moderna, Sanofi, Seqirus, Iliad, Dynavax, and GSK. TN is a member of COVID-19, Respiratory Syncytial Virus and influenza vaccines clinical trial committees conducted by Moderna, SKBio Korea, Clover (PRC), and Emergent Biotech, outside submitted work.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100815.

References

1 Whittaker C, Walker PGT, Alhaffar M, et al. Under-reporting of deaths limits our understanding of true burden of covid-19. *BMJ*. 2021;375:n2239.
2 Gibbons CL, Mangen MJJ, Plass D, et al. Measuring under-reporting and under-ascertainment in infectious disease datasets: a comparison of methods. *BMC Public Health*. 2014;14(1):147.
3 Gibney KB, Cheng AC, Hall R, Leder K. Australia's national notifiable diseases surveillance system 1991–2011: expanding, adapting and improving. *Epidemiol Infect*. 2017;145(5):1006–1017.
4 Crombie DL, Fleming DM, Cross KW, Lancashire RJ. Concurrence of monthly variations of mortality related to underlying cause in Europe. *J Epidemiol Community Health*. 1995;49(4):373–378.

5 von Cube M, Timsit JF, Schumacher M, et al. Quantification and interpretation of attributable mortality in core clinical infectious disease journals. *Lancet Infect Dis*. 2020;20(12):e299–e306.
6 Nguyen JL, Yang W, Ito K, et al. Seasonal influenza infections and cardiovascular disease mortality. *JAMA Cardiol*. 2016;1(3):274–281.
7 Schanzer DL, Tam TWS, Langley JM, Winchester BT. Influenza-attributable deaths, Canada 1990-1999. *Epidemiol Infect*. 2007;135(7):1109–1116.
8 Australian Institute of Health and Welfare. Deaths in Australia web report. Australian Government Department of Health. Australian Government; 2021. Available from: https://www.aihw.gov.au/reports/life-expectancy-death/deaths-in-australia/contents/summary. Accessed March 31, 2022.
9 Schmidt SSS, Iuliano AD, Vestergaard LS. All-cause versus cause-specific excess deaths for estimating influenza-associated mortality in Denmark, Spain, and the United States. *Influenza Other Respir Viruses*. 2022;16(4):707–716.
10 Rivera R, Rolke W. Modeling excess deaths after a natural disaster with application to hurricane maria. *Stat Med*. 2019;38(23):4545–4554.
11 Kontis V, Bennett JE, Rashid T, et al. Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries. *Nat Med*. 2020;26(12):1919–1928.
12 Fontela C, Aguinaga A, Moreno-Iribas C, et al. Trends and causes of mortality in a population-based cohort of HIV-infected adults in Spain: comparison with the general population. *Sci Rep*. 2020;10(1):8922.
13 Pedrazzoli D, Kranzer K, Thomas HL, Lalor MK. Trends and risk factors for death and excess all-cause mortality among notified tuberculosis patients in the UK: an analysis of surveillance data. *ERJ Open Res*. 2019;5(4):00125-2019.
14 Bollerup S, Hallager S, Engsig F, et al. Mortality and cause of death in persons with chronic hepatitis B virus infection versus healthy persons from the general population in Denmark. *J Viral Hepat*. 2022;29(9):727–736.
15 Helms M, Evans S, Vastrup P, et al. Short and long term mortality associated with foodborne bacterial gastrointestinal infections: registry based study. *BMJ*. 2003;326(7385):357.
16 Bilinski A, Thompson K, Emanuel E. COVID-19 and excess all-cause mortality in the US and 20 comparison countries, June 2021-March 2022. *JAMA*. 2023;329(1):92–94.
17 Rossen LM, Nørgaard SK, Sutton PD, et al. Excess all-cause mortality in the USA and Europe during the COVID-19 pandemic, 2020 and 2021. *Sci Rep*. 2022;12(1):18559.
18 Achilleos S, Quattrocchi A, Gabel J, et al. Excess all-cause mortality and COVID-19-related mortality: a temporal analysis in 22 countries, from January until August 2020. *Int J Epidemiol*. 2021;51(1):35–53.
19 Wang H, Paulson KR, Pease SA, et al. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-21. *Lancet*. 2022;399(10334):1513–1536.
20 Vanella P, Basellini U, Lange B. Assessing excess mortality in times of pandemics based on principal component analysis of weekly mortality data—the case of COVID-19. *Genus*. 2021;77(1):16.
21 Muscatello DJ, Amin J, MacIntyre CR, et al. Inaccurate ascertainment of morbidity and mortality due to influenza in administrative databases: a population-based record linkage study. *PLoS One*. 2014;9(5):e98446.
22 Adegboye OA, McBryde ES, Eisen DP. Tropical Australian health-data linkage shows excess mortality following severe infectious disease is present in the short-term and long-term after hospital discharge. *Healthcare (Basel)*. 2021;9(7):901.
23 *Public health and wellbeing Act, stat. 46 of 2008*. 2008. Available from: https://www.legislation.vic.gov.au/in-force/acts/public-health-and-wellbeing-act-2008/056.
24 *Birth deaths and marriages registration Act, stat. 43 of 1996*. 1996. Available from: https://www.legislation.vic.gov.au/in-force/acts/births-deaths-and-marriages-registration-act-1996/039.
25 Australian Bureau of Statistics. Life tables methodology 2021 [4/5/2022]. Available from: https://www.abs.gov.au/methodologies/life-tables-methodology/2018-2020#explanatory-notes.
26 Vandenbroucke JP. A shortcut method for calculating the 95 per cent confidence interval of the standardized mortality ratio. *Am J Epidemiol*. 1982;115(2):303–304.
27 Chen H, Matsumoto H, Horita N, et al. Prognostic factors for mortality in invasive pneumococcal disease in adult: a system review and meta-analysis. *Sci Rep*. 2021;11(1):11865.
28 Mungall BA, Hoet B, Nieto Guevara J, Soumahoro L. A systematic review of invasive pneumococcal disease vaccine failures and breakthrough with higher-valency pneumococcal conjugate vaccines in children. *Expert Rev Vaccines*. 2022;21(2):201–214.
29 Sings HL, De Wals P, Gessner BD, et al. Effectiveness of 13-valent pneumococcal conjugate vaccine against invasive disease caused by serotype 3 in children: a systematic review and meta-analysis of observational studies. *Clin Infect Dis*. 2018;68(12):2135–2143.
30 Ricketson LJ, Bettinger JA, Sadarangani M, et al. Vaccine effectiveness of the 7-valent and 13-valent pneumococcal conjugate vaccines in Canada: an IMPACT study. *Vaccine*. 2022;40(19):2733–2740.
31 Suzuki M, Dhoubhadel BG, Ishifuji T, et al. Serotype-specific effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumococcal pneumonia in adults aged 65 years or older: a multicentre, prospective, test-negative design study. *Lancet Infect Dis*. 2017;17(3):313–321.
32 McLaughlin JM, Jiang Q, Gessner BD, et al. Pneumococcal conjugate vaccine against serotype 3 pneumococcal pneumonia in adults: a systematic review and pooled analysis. *Vaccine*. 2019;37(43):6310–6316.
33 Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine and 20-valent pneumococcal conjugate vaccine among U.S. Adults: updated recommendations of the advisory committee on immunization practices - United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(4):109–117.
34 Australian Government Department of Health. *Pneumococcal polysaccharide conjugate vaccine, 15 valent adsorbed: 0.5 mL in pre-filled syringe; trade name TBC Australia*. Commonwealth of Australia. Australia Government Department of Health; 2022 [1/05/2022]. Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2021-11/pneumococcal-polysaccharide-conjugate-vaccine-15-valent-ads.
35 Sandvall B, Rueda AM, Musher DM. Long-term survival following pneumococcal pneumonia. *Clin Infect Dis*. 2013;56(8):1145–1146.
36 Johnstone J, Eurich DT, Majumdar SR, et al. Long-term morbidity and mortality after hospitalization with community-acquired pneumonia: a population-based cohort study. *Medicine*. 2008;87(6):329–334.
37 Winters BD, Eberlein M, Leung J, et al. Long-term mortality and quality of life in sepsis: a systematic review. *Crit Care Med*. 2010;38(5):1276–1283.
38 Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. *Am J Emerg Med*. 2020;38(7):1504–1507.
39 Heymann DL. *Control of communicable diseases manual: an official report of the American Public Health Association*. 18 ed. Washington DC: American Public Health Association; 2004.
40 Amin J, Law MG, Bartlett M, et al. Causes of death after diagnosis of hepatitis B or hepatitis C infection: a large community-based linkage study. *Lancet*. 2006;368:938–945.
41 Public Health England. *Hepatitis C: patient re-engagement exercise; information for GPs about the NHS England and public health England initiative to support finding and treating diagnosed patients*. UK: UK Government Digital Service; 2018. Available from: https://www.gov.uk/government/publications/hepatitis-c-patient-re-engagement-exercise.
42 Sempé L, Lloyd-Sherlock P, Martínez R, et al. Estimation of all-cause excess mortality by age-specific mortality patterns for countries with incomplete vital statistics: a population-based study of the case of Peru during the first wave of the COVID-19 pandemic. *Lancet Reg Health Am*. 2021;2:100039.