Public Health Wales Briefing:

All-cause mortality in nosocomial COVID-19 cases in Wales

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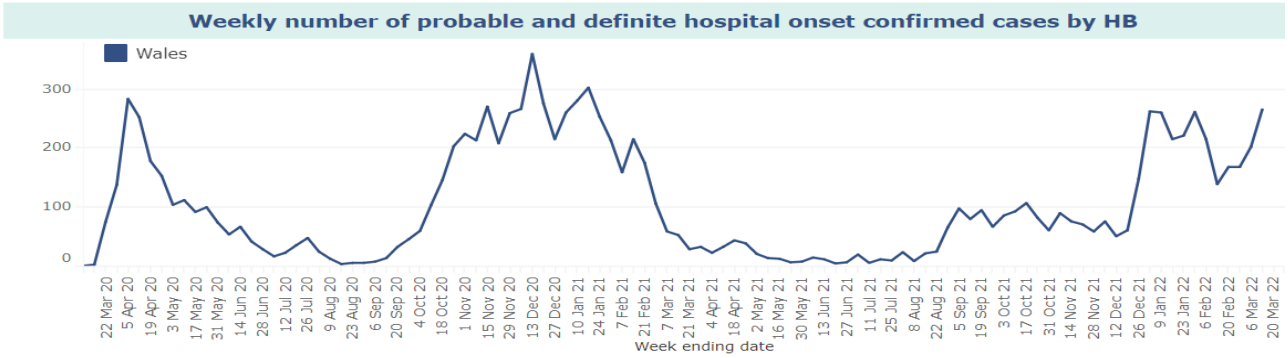
Background

Hospital acquired COVID-19 cases have contributed significantly to the burden of COVID-19 in hospitals in Wales, with increases in cases experienced within every pandemic wave (Fig 1). Overall, more than 10,000 probable or definite hospital acquired cases have been identified in Wales over the pandemic period. Nosocomial COVID-19 outbreaks have been associated with major disruption to hospital services, as well as with patient morbidity and mortality.

Figure 1. (1)



Deaths in patients with COVID-19 are an important measure of patient outcome and intervention success. Over the pandemic period we have seen improvements in patient management and treatments for COVID-19 disease, so would expect deaths to fall over time. Likewise, the development of effective vaccines and their high uptake, would also lead to reductions in deaths. Different variants of COVID-19 have been predominant at different times in the pandemic and some may be associated with lower disease severity. Data from both the ONS COVID-attributable death surveillance and the PHW Rapid Covid Mortality surveillance have shown downward trends in mortality over time (2).

Interpretation of crude death rates is complex in the context of the likely source of acquisition of COVID-19. We might expect higher death rates in patients with nosocomial COVID, since these patients have already been in hospital for more than a week prior to their positive test and are therefore likely to be in poorer general health and probably older than those with community acquired COVID-19. However, asymptomatic screening for COVID-19 has been routine practice in hospital settings since the second wave, so COVID-19 cases identified from screening may be associated with no clinical consequences of the infection and may have a lower risk of dying from COVID-19; it is not possible to distinguish between symptomatic and asymptomatic testing from centrally-held data. Community acquired cases admitted to hospital may differ in their acuteness of infection and their access to specialist healthcare may have been delayed. For both, the timing of their disease within the pandemic period and their vaccination status will also influence their outcome.

This report describes the 28-day all-cause mortality (ACM) by pandemic wave in patients likely to have nosocomial COVID-19 infections. It also provides a comparison of ACM between nosocomial cases and those likely to have acquired their infection in the community and subsequently admitted to hospital.

Methods

Data Sources

Public Health Wales Communicable Disease Surveillance Centre produces daily data on confirmed COVID-19 cases, based on an extract from the laboratory information management system (LIMS), via Datastore. Episodes are deduplicated on the basis of 42 days. This data is used as the starting point for surveillance of nosocomial COVID-19. Each confirmed case (based on a PCR test) is matched on NHS number with admission data from ICNet. The earliest admission date to the health board (where admission is continuous) is used for comparison with the specimen collection date.

Death data is also extracted from ICNet and date of death compared to date of positive test.

Data Extraction Date: 14/02/2022

Definitions

Nosocomial infections:

Definitions of nosocomial COVID-19 have been agreed across the UK based on the number of days between admission to the health board where the specimen was taken, and the date of specimen collection for the SARS-CoV-2 test. For patients in hospital:

- Non-hospital onset: specimens taken on day of admission or day after (days 1 and 2)
- Hospital onset, indeterminate healthcare associated: specimens taken on days 3 to 7 of admission
- Hospital onset, probable healthcare associated: specimens taken on days 8 to 14 of admission
- Hospital onset, healthcare associated: specimens taken >14 days after admission

Mortality: 28-day ACM – death due to any cause within 28 days of a positive SARS-CoV-2 test.

Waves:

- Wave 1 – 27/02/2020 - 26/07/2020
- Wave 2 – 27/07/2020 – 16/05/2021
- Wave 3 – 17/05/2021 – 19/12/2021
- Wave 4 – 20/12/2021 – 16/01/2022 (only cases where 28 days post positive specimen had elapsed at date of data extract were included)

Vaccination: Vaccination status at date of specimen was measured.

- Unvaccinated: No history of COVID-19 vaccination or first vaccination within the 14 days prior to the specimen date
- One dose: Specimen date more than 14 days after COVID-19 vaccination date with either no documentation of a second dose or the second dose was within the 14 days prior to the specimen date
- Two or more doses: Specimen date more than 14 days after date of second COVID-19 vaccination date

Model

A logistic regression model was developed to adjust for potential confounding in the comparison between acquisition categories. Each acquisition category was compared to the reference group of the non-hospital onset cases. Age group, sex, wave and vaccination status were included in the model; co-morbidities and COVID-19 related symptom status were not available for inclusion.

Results

- Overall, one quarter of patients with probable or definite nosocomial COVID-19 died within 28 days of their positive test (Table 1). Note that the cause of death may not have been COVID-19.
- The 28-day ACM in patients with nosocomial COVID-19 reduced with each subsequent wave of the pandemic (Table 1). In the first wave more than one third of patients died within 28 days of their positive test, compared to 13% in Wave 4 (Omicron).
- The 28-day ACM ranged from 24% to 28% in the major health boards, with all showing a downward trend across waves.

Table 1. 28-day ACM in probable and definite nosocomial COVID-19 cases in Wales by wave and by health board

	Wave 1		Wave 2		Wave 3		Wave 4		Total	
	Deaths n (%)	Cases n	Deaths n (%)	Cases n	Deaths n (%)	Cases n	Deaths n (%)	Cases n	Deaths n (%)	Cases n
Wales	**622 (34%)**	**1856**	**1428 (27%)**	**5236**	**245 (17%)**	**1476**	**113 (13%)**	**886**	**2408 (25%)**	**9,454**
Aneurin Bevan UHB	97 (40%)	244	255 (29%)	879	35 (18%)	192	6 (7%)	91	393 (28%)	1406
Betsi Cadwaladr UHB	199 (32%)	630	179 (25%)	705	41 (15%)	281	38 (14%)	264	457 (24%)	1880
Cardiff and Vale UHB	95 (31%)	303	210 (27%)	777	29 (18%)	166	12 (13%)	93	346 (26%)	1339
Cwm Taf Morgannwg UHB	115 (33%)	354	317 (28%)	1115	59 (18%)	327	16 (11%)	141	507 (26%)	1937
Hywel Dda UHB	25 (29%)	87	207 (39%)	694	50 (19%)	270	19 (13%)	148	301 (25%)	1199
Swansea Bay UHB	86 (40%)	214	243 (25%)	985	28 (16%)	180	21 (15%)	136	378 (25%)	1515

- The 28-day ACM was higher in nosocomial cases (25% probable and definite combined) than in cases who were identified on admission to hospital (22% non-hospital onset). (Table 2)

Table 2. 28-day ACM in COVID-19 cases in Wales by wave and by likely source of acquisition

	Wave 1		Wave 2		Wave 3		Wave 4		Total	
Acquisition	Deaths n (%)	Cases n	Deaths n (%)	Cases n	Deaths n (%)	Cases n	Deaths n (%)	Cases n	Deaths n (%)	Cases n
Non-hospital onset	507 (30%)	1,669	873 (25%)	3,569	378 (15%)	2,494	80 (12%)	682	1838 (22%)	8,414
Indeterminate hospital onset	168 (32%)	525	400 (29%)	1,366	85 (18%)	471	28 (13%)	215	681 (26%)	2,577
Probable hospital onset	249 (39%)	641	540 (30%)	1,810	70 (21%)	342	20 (10%)	202	879 (29%)	2,995
Definite hospital onset	373 (31%)	1,215	888 (26%)	3,426	175 (15%)	1,134	93 (14%)	684	1529 (24%)	6,459
Total	1297 (32%)	4,050	2701 (27%)	10,171	708 (16%)	4,441	221 (12%)	1,783	4927 (24%)	20,445

- Each hospital onset category was significantly associated with mortality compared to non-hospital onset cases on crude analysis. (Table 3)
- After statistical adjustment for any confounding effects of patient age, sex, vaccination status and pandemic wave, there was no evidence that cases who acquired COVID-19 in hospital were at increased risk of death compared to non- hospital onset cases. (Table 3)
- After statistical adjustment for confounding, older age, male sex, being unvaccinated and being diagnosed in the first wave remained significantly associated with mortality. The odds of death within 28 days in the over 85 year age group were 67 times higher than in the under 25 year age group and were 50% higher in males compared to females. There was a 40-50% decrease in the odds of death in vaccinated patients compared to unvaccinated and a 40% decrease in the odds of death in wave 4 compared to wave 1.

Table 3. Univariable and multivariable logistic regression results for 28-day ACM in hospital COVID-19 cases in Wales

Characteristic		Deaths n (%)	Cases n	Crude Odds Ratio (95% CI, p value)	Adjusted Odds Ratio (95% CI, p value)
Age group	0-24	9 (0.9%)	959	Ref	Ref
	25-44	38 (2.6%)	1,443	2.9 (1.4-6.3, <0.01)	3.1 (1.6-6.8, <0.01)
	45-64	441 (13.8%)	3,196	16.9 (9.3-35.5, <0.01)	16.9 (9.2-35.7, <0.01)
	65-74	888 (24.5%)	3,629	34.2 (18.8-71.6, <0.01)	36.3 (19.8-76.4, <0.01)
	75-84	1710 (29.2%)	5,858	43.5 (24.0-91.0, <0.01)	48.8 (26.6-102.5, <0.01)
	85+	1841 (34.3%)	5,360	55.2 (30.4-115.4, <0.01)	67.3 (36.8-141.5, <0.01)
Sex	Female	2168 (20.9%)	10,364	Ref	Ref
	Male	2759 (27.4%)	10,081	1.4 (1.3-1.5, <0.01)	1.5 (1.4-1.6, <0.01)
Wave	Wave 1	1297 (32.0%)	4,050	Ref	Ref
	Wave 2	2701 (26.6%)	10,171	0.8 (0.7-0.8, <0.01)	0.8 (0.8-0.9, <0.01)
	Wave 3	708 (15.9%)	4,441	0.4 (0.4-0.5, <0.01)	0.8 (0.7-1.0, 0.03)
	Wave 4	221 (12.4%)	1,783	0.3 (0.3-0.4, <0.01)	0.6 (0.5-0.7, <0.01)
Acquisition	Non-hospital	1838 (21.8%)	8,414	Ref	Ref
	Indeterminate	681 (26.4%)	2,577	1.3 (1.2-1.4, <0.01)	1.0 (0.9-1.0, 0.5)
	Probable	879 (29.3%)	2,995	1.5 (1.4-1.6, <0.01)	1.0 (0.9-1.1, 0.4)
	Definite	1529 (23.7%)	6,459	1.1 (1.0-1.2, <0.01)	0.8 (0.7-0.8, <0.01)
Vaccination status	Unvaccinated	167 (17.0%)	983	Ref	Ref
	1 Dose	772 (16.7%)	4,612	0.6 (0.5-0.7, <0.01)	0.5 (0.5-0.7, <0.01)
	≥2 Doses	3988 (26.9%)	14,850	0.6 (0.5-0.6, <0.01)	0.6 (0.5-0.7, <0.01)

Conclusions

Amongst more than 9000 patients with nosocomial COVID-19 in Wales analysed for this report, the ACM was 25%. This compares with 28% ACM in nosocomial cases in Scotland within a similar timeframe (to the end of December 2021) (3). This is considerably lower than some reports in the literature where ACM in nosocomial cases was more than 40% (4), but was based on patients with infections in the first wave. ACM in nosocomial patients in Wales was more than 30% in the first wave but has declined with each subsequent wave of the pandemic. A decline in ACM in each wave of the pandemic has been seen in all the major health boards, in addition to Wales as a whole.

Patients with nosocomial COVID-19 are likely to have other serious comorbidities warranting a stay in hospital of more than a week, which may mean they would have died irrespective of their COVID-19 infection. Likewise, patients with longer hospital stays are likely to be older and therefore more likely to die of other causes. Amongst hospitalised COVID-19 patients, we found no significant association between nosocomial acquisition and ACM, once potential confounding factors had been controlled for. Reports from the scientific literature are mixed as to whether nosocomial acquisition of COVID-19 is a risk factor for mortality. Studies have found a general increased risk associated with nosocomial acquisition (4), or in defined groups such as younger age groups (5) or cancer patients (6). Other investigations have found no significant differences in mortality between nosocomial and community acquired cases (7, 8), after controlling for confounders. Most studies available in the literature are based on earlier waves of the pandemic, whereas our analysis is based on cases from the start of the pandemic to mid January 2022. The Scotland report to the end of December also found no association between nosocomial acquisition and ACM, once potential confounding factors, including co-morbidities, had been controlled for (3).

From routine surveillance data available in Public Health Wales, it is not possible to distinguish between symptomatic patients and asymptomatic patients identified through the frequent routine screening that has taken place in hospital settings since the second wave. The exclusion of asymptomatic screening cases would give a more meaningful measure of outcomes associated with COVID-19 illness, if that became possible in the future. The reduced odds of mortality in definite nosocomial infections, may reflect an increased likelihood of long stay patients being picked up through regular asymptomatic screening. Comparisons of ACM between COVID-19 patients in hospital and hospitalised patients without COVID-19 during the pandemic period would also be an interesting as a future piece of work.

Factors that would be expected to be associated with mortality were found to be so in this data set, with significantly higher odds of death in older age groups and male patients. Vaccinated patients had a reduced odds of mortality compared to those unvaccinated. We were unable to see an increased benefit from multiple doses, but this may reflect measurement of ACM rather than COVID-19 attributable mortality. Each pandemic wave had reduced odds of mortality compared to the first, likely reflecting the improved treatment, patient management and availability of effective vaccination developed through the pandemic period, and perhaps reduced disease severity associated with different variants.

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