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Edited by Prof. R. Read

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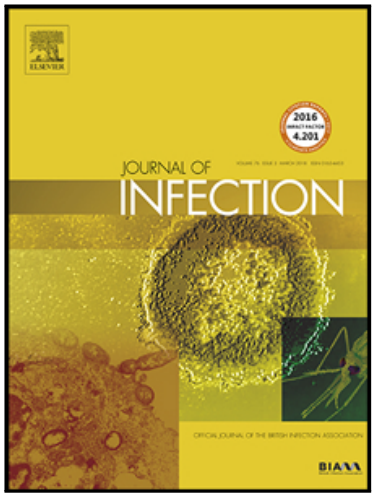

Evaluation of clinical harm associated with Omicron hospital-onset COVID-19 infection

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PII: S0163-4453(22)00628-4
DOI: https://doi.org/10.1016/j.jinf.2022.10.029
Reference: YJINF 5751

To appear in: *Journal of Infection*

Accepted date: 21 October 2022

Please cite this article as: Jonathan A. Otter , William Newsholme , Luke B. Snell , Blair Merrick , Nneoma Okeke , Damien J.F. Mack , Aodhán S Breathnach , Nicholas M Price , Evaluation of clinical harm associated with Omicron hospital-onset COVID-19 infection, *Journal of Infection* (2022), doi: https://doi.org/10.1016/j.jinf.2022.10.029

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Title: Evaluation of clinical harm associated with Omicron hospital-onset COVID-19 infection

Running title: Evaluation of Omicron COVID-19 harm

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Conflicts of interest: None

Funding sources: None.

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Highlights

- We reviewed outcomes for 129 patients with Omicron hospital-onset COVID-19 infection.
- 86 (66.7%) were asymptomatic; 15 (11.6%) had increased length of stay.
- 11 (8.5%) required supplemental oxygen, two (1.6%) required ICU or HDU.
- 3 (2.3%) had COVID-19 as a direct cause of death, and 4 (3.1%) where COVID-19 contributed.
- No associations between harm and age, vaccination, or vulnerability were found.

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The COVID-19 pandemic has seen waves of hospital-onset COVID-19 infection (HOCI).[1-3] As community prevalence rose and fell, so too did the prevalence of HOCI.[2, 3] COVID-19 waves in the UK can be characterised by the variants that caused them, with the 'Omicron wave' emerging in December 2021.[4] Outcomes in hospitalised patients with COVID-19 were poor pre-Omicron.[4-7] The Omicron variant resulted in a wave of HOCI in late 2021 and early 2022. A recent article in this journal found that 'incidental' COVID-19 infection was more common during the Omicron wave than the Delta wave, accounting for approximately two thirds of cases in one London hospital group.[1] We undertook an evaluation of harms associated with HOCI caused by Omicron in order to inform future decision making about COVID-19 risk management strategies.

We reviewed patients with probable HOCI (according to UK definitions) admitted to three London hospital groups between January and mid-March 2022. Patients with 'hospital-onset probable healthcare-associated' (HOPHA) (first positive specimen date 8-14 days after admission) and patients with 'hospital-onset definite healthcare-associated' (HODHA) (first positive >=15 days after admission) were included. Patients were from Guy's and St. Thomas' NHS Foundation Trust

(n=56), Royal Free London NHS Foundation Trust (n=49), and St. George's University Hospitals NHS Foundation Trust (n=24). These Trusts were testing all inpatients for SARS-CoV-2 two to three times each week, and had systems in place for real-time detection of HOCI. All COVID-19 during this period was assumed to the Omicron variant, supported by laboratory genotyping data. Patient notes and death certificates (where applicable) were reviewed and the following information was recorded: patient age, SARS-CoV-2 vaccination status, whether the patient is classified as 'vulnerable' as defined by a list used to determine eligibility for booster vaccination and treatment,[8] and whether or not the patient developed any symptoms consistent with COVID-19. The following measures of harm were chosen based on NHS guidance;[9] increased length of stay (>1 day) to manage their COVID-19 infection, new or increased requirement for supplemental oxygen, and admission to ICU or HDU for COVID-19. Death certificates of patients who died were reviewed to establish if COVID-19 was recorded as a direct cause of death (Part 1) or a condition contributing to the death (Part 2). Logistic regression was used to test whether any measure of harm (increased length of stay or new or increased requirement for supplemental oxygen or admission to ICU or HDU for COVID-19, or COVID-19 on Part 1 or Part 2 of the death certificate) was associated with age, patient vaccination status, or whether or not the patient was classified as clinically vulnerable. The review was considered service evaluation to help inform future infection prevention and control policy decisions.

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129 patients were included in the review (Table 1). 55 (42.6%) of patients were considered fully vaccinated (three doses), and 18 (14%) unvaccinated. 43 (33.3%) were considered vulnerable. 86 (66.7%) of patients did not develop symptoms of COVID-19. 15 (11.6%) patients had an increased length of stay, 11 (8.5%) had an increased oxygen requirement, and 2 (1.6%) required ICU or HDU attributed to COVID-19. Three (2.3%) patients had COVID-19 recorded as a direct cause of death (Part 1 of the death certificate), and four (3.1%) had COVID-19 recorded as a condition contributing to death (Part 2). A further 13 patients died but COVID-19 was not recorded on their death certificates. We did not identify any significant difference in age, vaccination status, or

clinically vulnerable status for the 21 patients for whom we recorded harm compared with 108 patients for whom we did not record harm.

Our findings suggest a step-change reduction in harms associated with HOCI caused by Omicron, which is consistent with the reduced harms attributed to Omicron elsewhere.[1,4] Despite one-third of patients being considered vulnerable to a poor outcome from COVID-19, only a small proportion of patients required escalation of care to ICU or HDU for COVID-19 (2%), or died from COVID-19 (2%), and the majority of patients were asymptomatic (67%). This contrasts previous waves, where outcomes for patients in hospital with COVID-19 were poor.[6, 10] Indeed, in one of our centres mortality from HOCI was around 30% during the first wave.[5] Also, a retrospective observational analysis including 374, 244 adult patients in England with COVID-19 in hospitals found that adjusted mortality rates fell from 40-50% in March 2020 to 11% in August 2020.[6] A review and meta-analysis found that mortality associated with nosocomial COVID-19 between January 2020 and February 2021 was significantly higher than for community infection.[7] A large study of around 1.5m patient in England found that Omicron COVID-19 was associated with a significantly lower risk of hospital attendance, hospital admission, and death, with the risk for all three measures approximately halved or more than halved.[4]

We did not identify associations between age, vaccination status, or clinical vulnerability status and clinical harm attributed to COVID-19. This is surprising because older age, incomplete vaccination, and underlying clinical vulnerability have been associated with clinical harm from COVID-19 with each previous wave.[4, 6, 7, 10] Whilst our dataset is small, our findings may be early evidence that these variables are less important in predicting harm associated with Omicron COVID-19 in hospitalised patients than for earlier variants.

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Our methods did not allow for direct comparisons of harms with previous COVID-19 variants. We also acknowledge some subjectivity in the attribution of harm, especially in deciding whether increased length of stay was due to medical care arising from COVID-19. We also only measured short-term harm associated with COVID-19, and didn't monitor long term clinical outcomes.

Our findings, from multiple hospital sites in London, suggest that when evaluating the utility of control measures for HOCI, it becomes more important to consider the indirect impacts of detecting and managing HOCI cases as the direct harms from HOCI fall. These indirect impacts include the burden of asymptomatic testing, subsequent impacts on individual patient management and discharge, and interruption to the flow of other patients due to contact isolation and bed closures.

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Table 1: Prevalence of symptoms and harm associated with COVID-19

COVID-19 symptoms	n	%
No	86	66.7
Yes	39	30.2
Unknown	4	3.1
Increased length of stay	n	%
No	109	84.5
Yes	15	11.6
Unknown	2	1.6
Increased O2	n	%
No	118	91.5
Yes	11	8.5
HDU/ICU admission	n	%
No	127	98.4
Yes	2	1.6
Outcome	n	%
Died by day 28 (COVID-19 not on death certificate)	13	10.1
Died by day 28 (COVID-19 on part 2 death of death certificate)	4	3.1
Died by day 28 (COVID-19 on part 1 death of death certificate)	3	2.3
Discharged or remained an inpatient at day 28	108	83.7
Unknown	1	0.8

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Table 2: Evaluation of associations with harm in patients with COVID-19

	Harm (n=21)		No harm (n=108)		p value
	n	%	N	%	
Age (median, range)	75 (55–91)	–	74 (11–96)	–	0.216
Vaccination status					
1st dose	1	4.8	3	2.8	0.698
2nd dose	8	38.1	35	32.4	0.858
3rd dose (or more)	7	33.3	48	44.4	0.674
Unknown	2	9.5	7	6.5	0.730
Unvaccinated	3	14.3	15	13.9	Ref
Clinically vulnerable					
Yes	5	23.8	38	35.2	0.316

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