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Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States

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Abstract. Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, Ibironke O, Hanna A, Ranski A, Halalau A (1From the Internal Medicine Department, Beaumont Health, Royal Oak, MI, USA). 2Internal Medicine Residents, Beaumont Hospital, Royal Oak, MI, USA). 3Oakland University William Beaumont School of Medicine, Rochester, MI, USA). 4Department of Medicine, Oakland University William Beaumont School of Medicine, Royal Oak, MI, USA). Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States (Rapid Communication). *J Intern Med* 2020; **288**: 469–476.

Introduction. Higher comorbidity and older age have been reported as correlates of poor outcomes in COVID-19 patients worldwide; however, US data are scarce. We evaluated mortality predictors of COVID-19 in a large cohort of hospitalized patients in the United States.

Design. Retrospective, multicenter cohort of inpatients diagnosed with COVID-19 by RT-PCR from 1 March to 17 April 2020 was performed, and outcome data evaluated from 1 March to 17 April 2020. Measures included demographics, comorbidities, clinical presentation, laboratory values and imaging on admission. Primary outcome was mortality. Secondary outcomes included length of stay, time to death and development of acute kidney injury in the first 48-h.

Results. The 1305 patients were hospitalized during the evaluation period. Mean age was 61.0 ± 16.3, 53.8% were male and 66.1% African American. Mean BMI was 33.2 ± 8.8 kg m^{-2}. Median Charlson Comorbidity Index (CCI) was 2 (1–4), and 72.6% of patients had at least one comorbidity, with hypertension (56.2%) and diabetes mellitus (30.1%) being the most prevalent. ACE-I/ARB use and NSAIDs use were widely prevalent (43.3% and 35.7%, respectively). Mortality occurred in 200 (15.3%) of patients with median time of 10 (6–14) days. Age > 60 (aOR: 1.93, 95% CI: 1.26–2.94) and CCI > 3 (aOR: 2.71, 95% CI: 1.85–3.97) were independently associated with mortality by multivariate analyses. NSAIDs and ACE-I/ARB use had no significant effects on renal failure in the first 48 h.

Conclusion. Advanced age and an increasing number of comorbidities are independent predictors of in-hospital mortality for COVID-19 patients. NSAIDs and ACE-I/ARB use prior to admission is not associated with renal failure or increased mortality.

Keywords: age, comorbidity, COVID-19, outcomes.

Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus first reported in December 2019, rapidly resulting in a global pandemic with over 5.4 million cases of novel coronavirus infection (COVID-19) globally as of May, 2020 [1]. Based on early data, it is estimated that in the United States and European Union, 80% of cases of COVID-19 result in mild illness, but 14% necessitate hospitalization, and 6% require intensive care unit (ICU) admission [2].

A large case series in New York City reporting on COVID-19 patients reported a Caucasian predominance, a median age of 63 years, hypertension as the

leading comorbidity and a high mortality rate of 21% [3]. We aimed to study patient demographics and their impact on in-hospital mortality in a large cohort of COVID-19 patients in southeast Michigan, USA, with the hypothesis that older age and increasing comorbidity are predictors of in-hospital mortality.

Methods

Dataset and population

Retrospective review of all inpatient records in Beaumont Health's eight hospitals was performed aiming to describe the epidemiologic and clinical characteristics of COVID-19 patients. Beaumont Health is the largest healthcare system in Southeast Michigan caring for over one-third of patients in the Detroit Metropolitan area. Individuals were included if they were hospitalized with SARS-CoV-2 infection demonstrated by a positive RT-PCR on nasopharyngeal swab per world health organization (WHO) guidance [4] between 1 March to 1 April 2020.

Variables

Data were abstracted through automated reports generated through Toad Data Point multi-platform database query tool from Beaumont's electronic medical record (EPIC System, Verona, WI, USA). Manual chart review was performed to confirm mortality to ensure accuracy and completeness. Variables abstracted included: demographics, comorbidities, clinical presentation, initial imaging findings, initial basic laboratory values, common medications and outcomes. Comorbidities were computed into the Charlson Comorbidity Index (CCI), a well-validated index that predicts risk of death within 1 year of hospitalization [5].

Outcomes

Primary outcome analysed was mortality. Secondary outcomes included Noninvasive ventilation (NIV) requirement defined as a need for bi-level airway pressure (BiPAP) or high flow nasal cannula (HFNC) support during admission, length of stay, intensive care unit admission, mechanical ventilation requirement and duration. Acute kidney injury (AKI) was defined per the KDIGO criteria for serum creatinine elevation > 0.3 mg dL^{-1} over 48 h [6].

Statistical analysis

Continuous data were reported as means and standard deviation (SD) or medians and interquartile range (IQR), and categorical variables as proportions. Logistic regression was used to evaluate univariate associations. Pertinent variables with *P*-values < 0.20 were included in the multivariate logistic regression model. All *P*-values were from 2-sided tests, and results were deemed statistically significant at $P < 0.05$. All statistical analyses were performed using International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) 25, (IBM Corporation: Armonk, NY, 10504).

Results

Demographics and comorbidities

A total of 1305 patients were analysed. Table 1 summarizes patient demographics and comorbidities. Mean age was 61.0 (16.3) years, 702 (53.8%) patients were male, 862 (66.1%) African American, 347 (26.6%) Caucasian and 90 (6.9%) of other ethnicities. Mean body mass index (BMI) was 33.2 (8.8) kg m^{-2}, and 54.0% of patients were non-smokers.

The most common comorbidity was hypertension (HTN) (56.2%), followed by diabetes mellitus (DM) (30.1%), and chronic kidney disease (CKD) (17.5%). 304 (23.3%) patients had one comorbidity, 20.8% had two, 14.0% had three, 12.9% had four or more comorbidities and 27.4% of patients had no comorbidities. Median CCI was 2 (1–4) for the cohort.

Angiotensin converting enzyme inhibitor (ACE-I) and angiotensin receptor blocker (ARB) use prior to admission was reported in 565 patients (43.4%) and nonsteroidal anti-inflammatory drugs (NSAIDs) use in 466 patients (35.7%).

Clinical features

Table 2 summarizes the clinical presentation, initial imaging and initial laboratory findings. Most common symptoms were cough (70.6%), fever (65.3%) and dyspnoea (63.4%). Median cough duration was 5 (2–7) days before admission. Other common symptoms include fatigue (36.1%), myalgias (22.6%), diarrhoea (18.9%) and nausea (17.2%).

Most common findings on initial chest X-ray were bilateral infiltrates/opacities (54.9%) followed by no infiltrates/opacities (27.6%) and unilateral infiltrates/opacities (17.4%). Similarly, chest

Table 1. *Demographic characteristics of hospitalized patients with novel coronavirus (COVID-19) infection*

Study population	No. (%)
Total Study Population	1305
Age, mean ± SD, y	61.0 ± 16.3
Male Sex	702 (53.8%)
Ethnicity (n = 1300)	
Caucasian	347 (26.6%)
African American	863 (66.1%)
Other	90 (6.9%)
Body Mass index, mean ± SD, kg m^{-2} (n = 1300)	33.2 ± 8.8
Smoking status (n = 1065)	
Former smoker	314 (24.1%)
Current smoker	42 (3.2%)
Never smoker	705 (54.0%)
Passive smoker	4 (0.3%)
Comorbidities	
Charlson Comorbidity Index (CCI), median (IQR)	2 (1–4)
Pulmonary comorbidities	
COPD	107 (8.2%)
Bronchial asthma	115 (8.8%)
OSA	116 (8.9%)
VTE	67 (5.1%)
Metabolic comorbidities	
Diabetes mellitus	393 (30.1%)
HTN	734 (56.2%)
Cardiac and renal comorbidities	
Coronary artery disease/peripheral artery disease	208 (15.9%)
Heart failure	75 (5.7%)
CKD	228 (17.5%)
Neurological comorbidities	
Cognitive impairment or Dementia	13 (1.0%)
CVA/TIA	95 (7.3%)
Other	
Chronic liver disease	6 (0.5%)
Cancer	83 (6.4%)
Immunosuppression	13 (1.0%)
Connective tissue disease	34 (2.6%)
Peptic ulcer disease	19 (1.5%)
No comorbidities	358 (27.4%)
Medications	
ACE-I or ARBs	565 (43.3%)
NSAIDs	466 (35.7%)

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; HLD, hyperlipidaemia; HTN, hypertension; No., number; NSAIDs, nonsteroidal anti-inflammatory medication; OSA, obstructive sleep apnoea; SD, standard deviation; TIA, transient ischaemic attack; VTE, venous thromboembolic disease; y, year

computed tomography (CT) showed bilateral infiltrates/opacities in 81.9% of patients, no infiltrates/opacities in 9.5% and unilateral infiltrates/opacities (8.6%).

Outcomes

Table 2 summarizes outcome data. As of 17 April 2020, 84 patients remain admitted. 200 (15.3%) patients died. Median time to death was 10 (6–14) days. Median length of stay (LOS) was 6 (3–10) days. ICU admission occurred in 344 (26.4%) patients, 276 (21.1%) required NIV, and 325 (24.9%) required mechanical ventilation with a median duration of 7 (4–13) days. AKI in the first 48 h was found in 76 (5.8%) patients.

Higher odds of mortality were present amongst patients older than 60 years (odds ratio (OR):3.66, 95% CI: 2.57–5.20), with a CCI > 3 (OR: 4.11, 95% CI: 3.00–5.62), CKD (OR: 1.86, 95% CI: 1.30–2.64), COPD (OR: 2.23, 95% CI: 1.41–3.52), HTN (OR: 1.43, 95% CI: 1.05–1.95), coronary artery disease/peripheral artery disease (CAD/PAD) (OR: 2.86,95% CI: 2.02–4.05), cancer (OR: 1.84, 95% CI: 1.09–3.11), cerebrovascular accident/transient ischaemic attack (CVA/TIA) (OR: 2.1, 95% CI: 1.30–3.43), venous thromboembolic disease (VTE) (OR: 1.80, 95% CI: 1.00–3.22) and ACE-I/ARB use (OR: 1.55, 95% CI: 1.15–2.10). Multivariate analysis utilized CCI as a surrogate for comorbidities. Age greater than 60 years (aOR: 1.93, 95% CI: 1.26–2.94) and CCI > 3 (aOR: 2.71, 95% CI: 1.85–3.97) were independent predictors of mortality.

Patients using NSAIDs prior to hospitalization had lower odds of mortality (OR: 0.55, 95% CI: 0.39–

Table 2. *Clinical Presentation, baseline investigations and outcomes of hospitalized Patients with Novel Coronavirus (COVID-19) Infection*

Initial presenting symptoms	No. (%)	Initial imaging findings		No (%)
Constitutional symptoms		*CXR findings*		1216 (93.2%)
Fever	852 (65.3%)	Unilateral infiltrate or opacities		212 (17.4%)
Chills	393 (30.1%)	Bilateral infiltrate or opacities		668 (54.9%)
Fatigue	471 (36.1%)	No infiltrate or opacities		336 (27.6%)
Anorexia	215 (16.5%)	Pleural effusion		96 (7.9%)
Malaise	87 (6.7%)	Pneumothorax		1 (0.1%)
Diaphoresis	45 (3.4%)	*Chest CT findings*		105 (8.0%)
Musculoskeletal symptoms		Unilateral opacities or infiltrates		9 (8.6%)
Myalgias	295 (22.6%)	Bilateral infiltrate or opacities		86 (81.9%)
Arthralgia	24 (1.8%)	No infiltrate or opacities		10 (9.5%)
Lower extremity swelling	22 (1.7%)	Pleural effusion		13 (1.9%)
Gastrointestinal		Pneumothorax		1 (1%)
Abdominal pain	108 (8.3%)	Pulmonary embolism		1 (1%)
Nausea	224 (17.2%)	*Initial Laboratory Values*	**Median (IQR)**	**No (%)**
Vomiting	161 (12.3%)	ALC, cells mm^{-3}	950 (323–605)	1274 (97.6%)
Diarrhoea	246 (18.9%)	AST, U L^{-1}	44 (29–67)	860 (65.9%)
Miscellaneous symptoms		ALT, U L^{-1}	28 (19–49)	860 (65.9%)
Dysgeusia, hypogeusia or ageusia	21 (1.6%)	ALP, U L^{-1}	70 (56–92)	1179 (90.3%)
Hyposmia, dysosmia or anosmia	111 (8.5%)	Total bilirubin, mg dL^{-1}	0.5 (0.4–0.8)	866 (66.4%)
Rash	1 (0.1%)	CRP, mg L^{-1}	115 (64.7–180.8)	865 (66.3%)
Upper respiratory tract symptoms		Creatine Kinase, U L^{-1}	230 (99–607)	609 (46.7%)
Sore throat	78 (6.0%)	LDH, U L^{-1}	432 (323–605)	757 (58.0%)
Rhinorrhea or nasal congestion	246 (18.9%)	Albumin, g L^{-1}	3.7 (3.4–4.0)	1195 (91.6%)
Lower Respiratory symptoms		Serum Creatinine, mg dL^{-1}	1.17 (0.92–1.64)	1275 (97.7%)
Cough	921 (70.6%)	Serum Procalcitonin, ng mL^{-1}	0.18 (0.08–0.48)	826 (63.3%)
Duration of cough, median (IQR), d	5 (2–7)	Prothrombin time/s	13.2 (12.4–14.4)	634 (48.6%)
Sputum Production	96 (7.4%)	Activated PTT/s	33.1 (30.2–37.5)	614 (47.0%)
Hemoptysis	79 (6.1%)	D-Dimer, ng mL^{-1}	1148 (680–2527)	442 (33.9%)
Dyspnoea	827 (63.4%)	PaO2/FiO2 ratio	103 (69–187)	281 (21.5%)
Chest pain	163 (12.5%)	*Outcomes (No = 1305)*		
Paroxysmal nocturnal dyspnoea	5 (0.4%)	NIV requirement		276 (21.1%)
Neurological symptoms		AKI in first 48 h		76 (5.8%)
Headache	115 (8.8%)	ICU Admission		344 (26.4%)
Confusion	97 (7.4%)	Mechanical ventilation requirement		325 (24.9%)

Table 2 (*Continued*)

Initial presenting symptoms	No. (%)	Initial imaging findings		No (%)
Dizziness	35 (2.7%)	Duration of mechanical ventilation, median (IQR), d	7 (4–13)	
Lightheadedness	68 (5.2%)	Length of stay, median (IQR), d	6 (3–10)	
Syncope	56 (4.3%)	Mortality		200 (15.3%)
		Time to death, median (IQR), d	10 (6–14)	

AKI, acute kidney injury; ALC, absolute lymphocyte count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; CT, computed tomography; CXR, chest X-ray; d, days; ICU: intensive care unit; IQR: interquartile range; IQR: interquartile range; LDH, Lactate dehydrogenase; NIV, noninvasive ventilation; No., number; PTT: partial thromboplastin time; s: seconds; SD, standard deviation

0.78). This finding was present on multivariate regression analysis (aOR: 0.56, 95% CI: 0.40–0.82).

Mortality did not differ significantly with sex, race, smoking history, BMI, type of infiltrates or absence of infiltrates on chest imaging, DM, heart failure, obstructive sleep apnoea, asthma, chronic liver disease, dementia, immunosuppression, peptic ulcer disease or connective tissue disease. ACE-I/ARB use was not associated with increased mortality on multivariate analysis.

Only initial serum creatinine was found to be an independent predictor of AKI (aOR: 1.2, 95% CI: 1.1–1.30). Age > 60, sex, race, smoking history, BMI, DM, NSAID use and ACE-I/ARB use were not associated with an increased risk of AKI in the first 48 h. CCI > 3, HTN and CKD were associated with increased AKI risk on univariate analysis but were not significant on multivariate analysis ($P = 0.200$, $P = 0.324$, $P = 0.357$, respectively). These results are summarized in Table 3.

Discussion

In this large cohort of hospitalized COVID-19 patients, 66.1% were African American, averaging 61 years of age, with a slight male predominance. The age and sex demographics appear similar to a 5700-patient cohort from NYC (63 years, 60.3% males); however, only 22.6% of the latter cohort were African American [3]. HTN was the most common comorbidity in our study followed by DM and CKD. More than half of the cohort had at least one comorbidity, and an average BMI of 33.2 kg m^{-2}. Comorbid pulmonary conditions were reported in less than 10% of the cohort. This could be due to underreporting or underdocumentation in the electronic medical record. Overall, obese, older male patients with multiple comorbidities have been reported to have greater disease severity warranting hospitalization [3, 7].

Thirty symptoms were evaluated on presentation, and cough, dyspnoea, fever, and fatigue were the most common, similar to other cohorts [8–10]. Diarrhoea was the most common gastrointestinal manifestation in 18.9% of patients, and more common than other cohorts [10-11]. In contrast to studies in Italy, lower ICU admission and mechanical ventilation rates were noted in our cohort despite similar age, demographics and comorbidity [12]. This could be explained by different criteria for ICU admission in different countries and prevalent use of NIV in our cohort on non-ICU floors.

Data reported by the American public media (APM) research laboratories suggest a large disparity in mortality amongst African Americans in Michigan, with 45% of deaths occurring in African Americans who constitute only 17% of Michigan's population [13]. Our cohort demonstrated no significant racial association with mortality amongst hospitalized patients. In line with multiple studies [7, 14-15], our cohort demonstrates that medical comorbidity confers a worse prognosis in an incremental fashion. A CCI > 3 independently predicted 2.71 increased mortality odds, and patients with CAD/PAD or COPD had 2.86 and 2.23 increased mortality odds, respectively. Additionally, older age is an independent predictor of mortality. Age-dependent defects in immune cells leading to a more robust inflammatory response have been suggested as a theory for higher mortality in the elderly [16].

Table 3. *Statistical analysis of demographic, comorbidity and imaging indices amongst mortality cases and patients developing acute kidney injury (AKI) in the first 48 h*

Mortality			AKI in first 48 h	
Univariate analysis	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Demographics				
Age > 60 vs. Age < 60 years	3.66 (2.57–5.20)	0.000	0.92 (0.58–1.48)	0.738
Sex	0.96 (0.71–1.3)	0.807	1.06 (0.66–1.70)	0.817
Caucasian race	1.01 (0.53–1.91)	0.977	1.39 (0.48–3.98)	0.545
Other race	1.70 (0.88–3.30)	0.115	1.22 (0.40–3.72)	0.732
Smoking history	1.19 (0.55–2.60)	0.660	1.19 (0.55–2.60)	0.660
Body Mass Index (BMI)	0.99 (0.97–1.01)	0.154	0.46 (0.99–1.04)	0.459
Medications				
NSAID use	0.55 (0.39–0.78)	0.001	0.84 (0.51–1.39)	0.492
ACE-I/ARB use	1.55 (1.15–2.10)	0.004	1.11 (0.69–1.79)	0.656
Comorbidities				
CCI > 3 *vs.* CCI < 3	4.11 (3.00–5.62)	0.000	1.75 (1.09–2.81)	0.021
HTN	1.43 (1.05–1.95)	0.025	1.70 (1.02–2.82)	0.043
DM	1.24 (0.90–1.70)	0.194	1.43 (0.88–2.33)	0.148
CKD	1.86 (1.30–2.64)	0.001	2.86 (1.73–4.73)	0.000
COPD	2.23 (1.41–3.52)	0.001	–	–
CAD/PAD	2.86 (2.02–4.05)	0.000	–	–
Cancer	1.84 (1.09–3.11)	0.024	–	–
Heart Failure	1.68 (0.96–2.94)	0.072	–	–
OSA	1.17 (0.70–1.94)	0.549	–	–
Bronchial Asthma	1.18 (0.71–1.96)	0.520	–	–
CVA or TIA	2.11 (1.30–3.43)	0.002	–	–
Chronic Liver Disease	2.78 (0.51–15.3)	0.240	–	–
VTE	1.80 (1.00–3.22)	0.049	–	–
Dementia	1.01 (0.22–4.57)	0.995	–	–
Immunosuppression	2.49 (0.76–8.15)	0.133	–	–
Peptic Ulcer Disease	1.03 (0.30–3.55)	0.969	–	–
Connective Tissue Disease	1.45 (0.62–3.37)	0.391	–	–
Imaging Findings				
Unilateral infiltrates/opacities on CXR	0.78 (0.49–1.23)	0.278	–	–
Bilateral infiltrates/opacities on CXR	0.87 (0.58–1.30)	0.481	–	–
Infiltrates/opacities on chest CT	1.05 (0.12–9.32)	0.963	–	–
Laboratory values				
Initial Serum Creatinine, mg dL^{-1}	–	–	1.23 (1.14–1.33)	.000

Variable	aOR (95% CI)	*P* value	Variable	aOR (95% CI), *P*-value
Multivariate analysis				
Age > 60 *vs.* Age < 60 years	1.93 (1.26–2.94)	0.002	Initial Serum Creatinine, mg dL^{-1}	1.2 (1.1–1.30), 0.000
CCI > 3 *vs.* CCI < 3	2.71 (1.85-3.97)	0.000	CCI > 3 vs. CCI < 3	1.41 (0.83–2.38), 0.200

Table 3 (*Continued*)

Variable	aOR (95% CI)	*P* value	Variable	aOR (95% CI), *P*-value
NSAID use	0.57 (0.40–0.82)	0.002	HTN	1.32 (0.76–2.30), 0.324
ACE-I/ARB use	1.20 (0.86–1.68)	0.278	CKD	1.35 (0.72–2.54), 0.357

ACE-I, angiotensin converting enzyme inhibitor; AKI, acute kidney injury; aOR, adjusted odds ratio; ARB, angiotensin receptor blocker; CAD, coronary artery disease; CCI, Charlson Comorbidity Index; CI, confidence interval; CKD, chronic kidney disease; COPD: chronic obstructive pulmonary disease; CT, computed tomography; CVA, cerebrovascular accident; CXR, chest X-ray; HTN, hypertension; NSAIDs: nonsteroidal anti-inflammatory medication; OSA: obstructive sleep apnoea; PAD, peripheral artery disease; TIA, transient ischaemic attack; VTE, venous thromboembolic disease.

SARS-CoV-2 utilizes the ACE2 receptor as a site for viral cell entry [17] which is upregulated by ACE-I and NSAIDs. No data exist to date correlating SARS-CoV-2 infection rate with ACE2 levels in vivo. ACE-I/ARB use was associated with no increased mortality or early AKI development in our cohort and has been suggested to have protective effects in other cohorts [18]. This suggests the relative safety of using these agents in individuals at risk of contracting SARS-CoV-2.

Interestingly, NSAID use was correlated with lower mortality odds even when controlling for other predictors in our cohort. Indomethacin has reported in vivo anti-viral replication properties in SARS-CoV-1 in canines [19]. A number of clinical trials are evaluating different NSAIDs in COVID-19 treatment in light of their anti-inflammatory and possible anti-viral properties [20, 21]. However, insufficient data currently exist to recommend for or against NSAID use for COVID-19 treatment.

Major limitations in our study include its retrospective design, short follow-up time and its applicability only to a hospitalized population.

Conclusion

Our study suggests older age and medical comorbidity as independent predictors of in-hospital mortality in COVID-19 patients. NSAID and ACE-I/ARB use prior to hospitalization is not associated with early AKI or increased mortality.

Conflict of Interest

None.

Author Contributions

Zaid Imam: Data curation (equal); Formal analysis (lead); Investigation (equal); Methodology (supporting); Writing-original draft (equal); Writing-review & editing (equal). **Fadi Odish:** Conceptualization (supporting); Data curation (equal); Formal analysis (supporting); Writing-original draft (equal); Writing-review & editing (equal). **Inayat Gill:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Daniel O'Connor:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Justin Armstrong:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Aimen Vanood:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Oluwatoyin Ibironke:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Angy Hanna:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Alexandra Ranski:** Data curation (equal); Writing-original draft (equal); Writing-review & editing (equal). **Alexandra Halalau:** Conceptualization (lead); Formal analysis (equal); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (lead); Supervision (lead); Validation (lead); Visualization (lead); Writing-original draft (equal); Writing-review & editing (lead).

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