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Scientific Article

From Alpha to Omicron: A Radiation Oncology Network's Biocontainment-Based COVID-19 Experience

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Abstract

Purpose: To develop the safest possible environment for treating urgent patients with COVID-19 requiring radiation, we describe the unique construction of negative air pressure computed tomography simulator and linear accelerator treatment vaults in addition to screening, delay, and treatment protocols and their evolution over the course of the COVID-19 pandemic.

Methods and Materials: Construction of large high-efficiency particulate air filter air-flow systems into existing ductwork in computed tomography simulator rooms and photon and proton treatment vaults was completed to create negative-pressure rooms. An asymptomatic COVID-19 screening protocol was implemented for all patients before initiation of treatment. Patients could undergo simulation and/or treatment in the biocontainment environments according to a predefined priority scale and protocol. Patients treated under the COVID-19 protocol from June 2020 to January 2022 were retrospectively reviewed.

Results: Negative air-flow environments were created across a regional network, including a multi-gantry proton therapy unit. In total, 6525 patients were treated from June 2020 through January 2022 across 5 separate centers. The majority of patients with COVID-19 had radiation treatment deferred when deemed safe. A total of 42 patients with COVID-19, who were at highest risk of an adverse outcome should there be a radiation delay, were treated under the COVID-19 biocontainment protocol in contrast to those who were placed on treatment break. For 61.9% of patients, these safety measures mitigated an extended break during treatment. The majority of patients (64.3%) were treated with curative intent. The median number of biocontainment sessions required by each patient was 6 (range, 1-15) before COVID-19 clearance and resumption of treatment in a normal air-flow environment.

Conclusions: Constructing negative-pressure environments and developing a COVID-19 biocontainment treatment protocol allowed for the safe treatment of urgent radiation oncology patients with COVID-19 within our department and strengthens

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future biopreparedness. These biocontainment units set a high standard of safety in radiation oncology during the current or for any future infectious outbreak.

Introduction

During the SARS-CoV-2 pandemic, the medical field was forced to rapidly reconstruct and reorganize the delivery of patient care. While the initial response of many hospitals was to severely limit—if not completely halt—elective outpatient procedures and visits, the delivery of cancer care was challenged in unique ways, given the necessity to conduct lifesaving cancer treatment as soon as possible. In the field of radiation oncology and beyond, this led to a swift response, including the adoption of telemedicine,[1] the publication of consensus guidelines for cancer management during the pandemic,[2-4] and the shift to virtual medical student clerkships and residency interviews.[5,6]

In immunocompromised patients with cancer, the delicate balance of treating life-limiting malignancies and risk of COVID-19 infection was studied early in the pandemic in the prevaccination era. Initial data indicated that combining cancer care and COVID-19 therapy simultaneously resulted in poor outcomes and that delaying cancer care until COVID-19 symptoms had resolved resulted in better outcomes.[7] Therefore, most patients with a COVID-19 diagnosis had radiation treatment delayed for a minimum of 2 or more weeks. However, it was clear that radiation therapy was a resource that needed to remain available and accessible to patients in the safest manner possible. Many clinics adopted the paradigm of treating patients at the end of the day when known to be positive. However, over the course of the pandemic, the virulence of SARS-COV-2 variants increased, resulting in high risk for unintended spread of the virus from asymptomatic patients to others. Confined spaces within the radiation oncology clinic such as the simulator and linear accelerator vaults required select patients (eg, patients with head and neck cancer) to remove their N95 or surgical face mask to have an immobilization mask placed for treatment. For asymptomatic patients with COVID-19, this would result in contaminated air space and a risk of heightened infectivity from a patient unaware of their COVID-19 status to another patient or staff member. In an attempt to maximize safety, we implemented asymptomatic testing and the construction of biocontainment negative-air-flow spaces to minimize the spread of COVID-19 to set the highest standard of care that could be achieved.

The Johns Hopkins Medicine Radiation Oncology network comprises 5 hospitals spanning Baltimore, MD (3 sites), Bethesda, MD (1 site), and Washington, DC, (1 site) in the United States, which includes 6 computed tomography (CT) simulators, 13 photon-based linear accelerators, and 3 proton therapy gantries. In collaboration with our Hospital Epidemiology and Infection Control (HEIC) colleagues, we implemented asymptomatic screening protocols for patients initiating radiation therapy and developed a COVID-19 biocontainment treatment protocol after construction of a negative pressure CT simulator room and linear accelerator treatment vault environments at our main campus early in the pandemic, a biopreparedness effort which expanded after subsequent waves of variants resulted in high infection rates despite booster vaccination.

Methods and Materials

Creating negative-pressure CT simulator rooms and treatment vaults

In April 2020, an engineering project manager reviewed existing rooms and ventilation system/air flows within our main campus clinic in conjunction with HEIC. One CT simulator room and one linear accelerator treatment vault at Johns Hopkins Hospital were chosen based on size and location within the department as pilot areas to provide negative air-flow environments to ensure the safe treatment of patients with COVID-19 in the prevaccination era. Importantly, the selected vault housed a linear accelerator that was most compatible with other machines both at the main campus and at our regional campuses in effort to facilitate a smooth transition of patient care with minimal replanning requirements. Patients suspected of or positive for COVID-19 infection were treated at the end of the day followed by a terminal clean.

The simulator room was minimally negative pressure (27.99 air exchange per hour) and the addition of a high-efficiency particular air (HEPA) filter increased this level. An adjacent doffing area needed to be constructed to reduce the risk of health care worker infection. The linear accelerator vault was positive pressure (5.94 air exchanges per hour) and required placement of 2 HEPA filters to convert the room into negative pressure and to HEPA-filter the air before returning to the air handling units that supply the rest of the building. The treatment vault space did not allow for building a donning and doffing area inside the room, so a separate area was built outside the vault. The control panel to operate the door to the treatment vault needed to be relocated so it could be operated outside of the donning and doffing area. Given the proximity of the documentation/operations alcove to the donning and doffing area, personnel were recommended to wear respirators, such as N95s, while stationed there regardless of whether they directly interacted with the patients with COVID-19 or person under investigation (PUI) patients. All negative air-flow was managed via on-off switches for the HEPA filters, thereby allowing maximal flexibility in utilization and necessity for patient care. Early in the pandemic, patients were transferred to the main campus at Johns Hopkins Hospital for treatment when COVID-19 positive to ensure the safety of patients without COVID-19.

In December 2021, in response to the Omicron variant surge, biocontainment construction was expanded to 2 of our higher-volume regional campuses to increase access to care without need for treatment relocation. This included construction projects at our Washington DC-based proton and photon facility at Sibley Memorial Hospital, as well as our Bayview Hospital campus in Baltimore, MD, which focuses on thoracic oncology. Similar to the main campus, HEIC assessed the air flow/air filtration systems to determine number of HEPA filters required to create negative pressure environments, and surveyed the clinics to recommend the modifications necessary to build suitable donning and doffing spaces. Representative construction schematics and photos of the HEPA filtration systems are shown in Figs. E2 and E3, respectively.

Implementing a COVID-19 screening and testing protocol

In May 2020, all sites of the radiation oncology department at Johns Hopkins transitioned from a daily symptomatic screening algorithm to an asymptomatic test-based protocol for all patients scheduled for treatment in radiation oncology, in following with the institution's approach to elective (ie, nonemergent) outpatient procedures. Asymptomatic SARS-Cov-2 molecular testing was strongly recommended for all patients within 7 days before starting treatment. Nursing staff maintained updated screening results for each patient, as some patients obtained tests outside of our hospital system. Documented COVID-19 testing result or note indicating that the patient declined screening was added as a line item on the new start checklist for radiation therapists. A minority of the 5197 total new-start patients (52) from May 18, 2020, to September 7, 2021, (when the universal asymptomatic screening policy was discontinued) declined testing per review of therapy documentation. On January 3, 2022, in response to the surge of the Omicron variant, an asymptomatic testing program was implemented for patients whose treatments require removal of face masks (ie, patients whose immobilization involves aquaplast masks or breath-hold techniques). These patients were recommended to be tested before treatment and up to weekly while on treatment at the discretion of the treating physician.

If a patient tested positive on either asymptomatic or symptomatic testing, the attending physicians considered delay until clearance of COVID-19 isolation precautions based on institutional policy. A retesting strategy for clearance (recommended for severely immunocompromised patients) required either 2 consecutive negative tests or a single negative test at 28 days after documented positivity, while a nonretesting strategy necessitated at minimum 10 to 14 days of quarantine after the positive test with improvement or resolution of symptoms. Alternatively, patients with COVID-19 could be considered for treatment and/or simulation in our newly constructed biocontainment environments per attending discretion with the guidance of a predefined priority scale and consideration of patient preference. Before the more recent expansion of biocontainment resources at select regional campuses, if a patient with COVID-19 was identified from a regional campus, the attending could elect to transfer the treatment plan to the main campus at Johns Hopkins Hospital in Baltimore, MD. Figure E1 details the algorithm for our testing strategy and the management of patients with COVID-19 after (1) implementation of universal asymptomatic testing before treatment and (2) biocontainment simulation/treatment capabilities were available at the main campus. Special consideration for utilization of biocontainment resources was also applied to patients designated as PUI, particularly if this involved continued close household exposures.

Preparing clinical staff for the care of patients with COVID-19

To prepare nursing and therapy staff to care for patients with COVID-19, a training program was implemented that included several important safety components. Clinical staff caring for patients in our negative pressure rooms were provided video and in-person training on donning and doffing personal protective equipment (PPE). Several training drills were conducted with all team members anticipated to facilitate treatment of patients with COVID-19 to help them better understand the detailed steps required to keep both patients and staff safe. Completion of 3 drills per staff member was required for competency. This, in particular, involved establishing and practicing a safe pathway to escort the patient from their transportation vehicle directly to the treatment room and vice versa. Patients treated under the COVID-19 biocontainment protocol were scheduled for the last treatment slot of the day, allowing for proper terminal cleaning by environmental services and to minimize the risk of exposing other patients.

A clear delineation of roles for each individual on the COVID-19 protocol treatment team was emphasized. The

Table 1 Responsibilities of each role in the COVID-19 protocol simulation and treatment of patients

Safety officer	Indirect contact therapist	Direct contact therapist
	Set HEPA filter to "high" in donning/doffing spaces during setup	
Ensure that all necessary items are present in donning and doffing space	Set up Ascom phone and place in "clean space" of doffing area for safety officer's use and communication	Perform smoke test to ensure room functioning properly at negative pressure
Review patient route to ensure halls cleared of obstacles	Communicate through intercom to direct contact therapist to confirm setup, directing manual shifts, etc	Walk patient to and from the room under the guidance of the safety officer
Ensure the treatment vault waiting room and walkway is clear of all patients	Communicate with environmental services and post terminal cleaning signs once patient has left	Explain procedures to the patient and confirm 2 patient identifiers daily (date of birth and treatment identification card)
Open and close all doors	Perform all computer work (to include assessments, site setup, checklists, imaging, shifting, treatment, etc)	Align patient into position and make required manual shifts as necessary
Communicate with indirect and direct contact therapists from doffing space using Ascom phone	Simulation only: take patient setup photo through window	Lead the timeout inside the room through the intercom
Supervise direct contact therapist donning and doffing		Clean and bag immobilization devices before patient exits the room
		Bag all linen, tied tight, to be left in the room overnight for Environmental Services to remove

Abbreviation: HEPA = high-efficiency particular air.

safety officer did not have a direct patient care component and instead ensured that the patient with COVID-19 could travel safely within the department, that negative pressure rooms were functioning as intended, and that PPE was properly donned and doffed. A two-member radiation therapist team was scheduled for each COVID-19 protocol treatment. The "indirect contact" therapist remained in the control room to instruct and confirm setup shifts, while the "direct contact" therapist actively interacted with the patient in the treatment vault for physical setup and manual shifts. Both the safety officer and the direct contact therapist wore full PPE, while the indirect contact therapist wore at minimum a respirator, such as an N95 mask. The specific responsibilities for each role are further detailed in Table 1. The preparation checklist shown in Fig. 1 was reviewed by the 3 members of the treatment team in a huddle before each COVID-19 protocol treatment.

Results

The treatment of patients with COVID-19 evolved over the course of the pandemic. Figure 2 details the timeline of major events in our COVID-19 screening and biocontainment response. Construction of the biocontainment units was the first and most immediate need to ensure the highest safety and infection control standards were met within radiation oncology. This was followed by implementing a screening protocol to ensure accurate identification of patients with COVID-19 in the prevaccination era, and later, to screen based on the increased risk of infection due to variant COVID-19 strains even in those vaccinated. A total of 6525 patients were treated from June 2020 through January 2022 across 5 sites as part of an integrated radiation oncology network. During this time, while the majority of patients with COVID-19 underwent treatment delays, 42 patients who met criteria by protocol[8] were simulated and/or treated under the COVID-19 biocontainment protocol. The median age of these patients was 61 years (range, 3-83). Fifteen patients (35.7%) were transferred from a regional campus to the main campus for management due to COVID-19 positivity. This included 2 pediatric patients with Wilm tumors for whom it was felt treatment initiation could not be delayed. Importantly, 27 patients (64.3%) were treated with a curative intent, while 10 patients (23.8%) were treated as a result of an inpatient palliative consult. The majority of patients (61.9%) were initiated on the COVID-19 protocol after they were already midway into their intended treatment course, with 6 of these patients requiring hospital admission for their COVID-19 infections. Two patients were converted to COVID-19 protocol after becoming a PUI during their treatment courses due to continued close COVID-19−positive contacts in their household, although quarantine from these individuals was advised as much as feasible. While the most common indication for initiating the COVID-19 biocontainment protocol was to mitigate a long treatment break in patients who had already initiated

COVID-19 TREATMENT CHECKLIST

- ☐ Patient called previous day– review parking location, what to expect from staff, and symptoms
- ☐ Who's on the team today? Date ____________________
    - o "Direct Contact Therapist"____________________________
    - o "Indirect Contact Therapist"____________________________
- ☐ Who is the Safety Officer today?____________________
- ☐ Safety Officer number______________________________
- ☐ Barcode printed out for patient
- ☐ Personal sharpie needed for patient setup
- ☐ Does the donning space have hand sanitizer and all of the PPE needed (Gowns, Gloves, Face Shield, N95)?
- ☐ Does the doffing space have hand sanitizer, trashcan, purple top wipes and place to set face shield to be cleaned?
- ☐ Signs posted in designated spaces of doffing/donning areas
- ☐ (Ascom) Phone # _________________ (from nurses station for 2-way communication between Direct and Indirect Contact Therapists)
- ☐ Terminal clean number and sign out sheet posted and signed
- ☐ Email sent and called over to Environmental Services for terminal cleaning
- ☐ Empty treatment room of ALL items that can be removed or hidden behind cabinet doors, cover hand pendants with plastic bag (loosely)
- ☐ HEPA filter setting on HIGH/Doors Closed to Doffing Spaces
- ☐ Gown available for patient to change into
- ☐ Have ALL supplies out to be used for patient appointment (i.e., aquaplast, memory foam, lubricating jelly, linen bag etc.)
- ☐ Late Attending, Resident & Physicist notified
- ☐ Physician available and ready to review images if needed
- ☐ (Sim only) Unlock scanner room door
- ☐ (Sim only) Lock back simulation room entrance by the bathroom and hang sign (Sim only)
- ☐ Smoke Test Completed ______________________(Follow Frequency Per Smoke Test Written Procedure)
- ☐ Review "Responsibilities" and "Think Ahead Items"

Figure 1 Checklist to be completed with every COVID-19 protocol treatment.

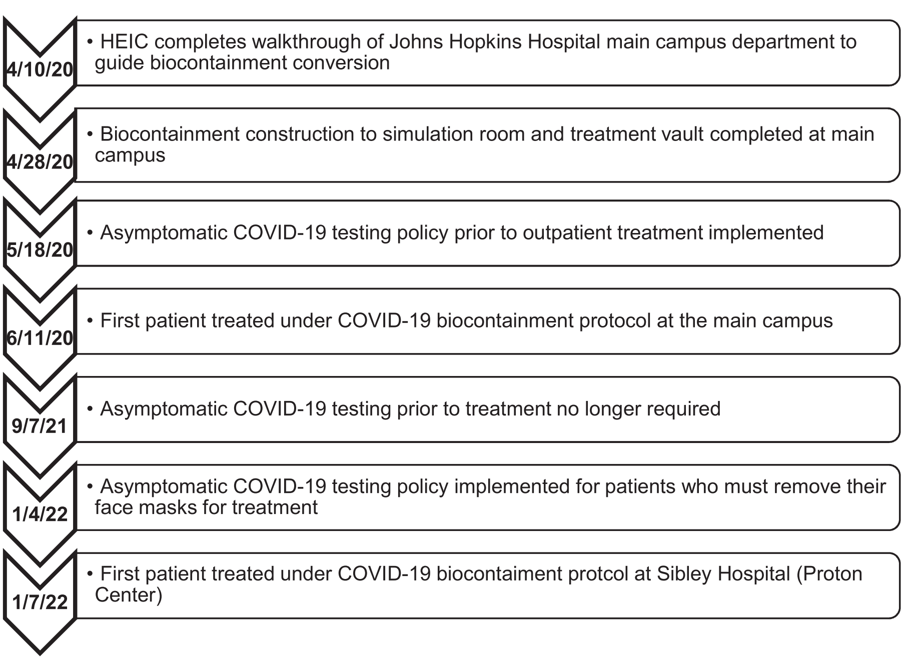

Figure 2 Timeline of key events.

their curative intent treatment course, there were also several palliative cases to address symptoms such as intractable pain (6 cases) and bleeding (3 cases). One case resulted from an urgent inpatient consult to consider radiation therapy for heterotopic ossification prophylaxis in an incidentally COVID-19−positive patient who required emergent surgery for a severe fracture sustained from a motor vehicle accident. Though prophylactic in nature, the tight window of efficacy for radiation therapy in heterotopic ossification prophylaxis precluded this patient from otherwise being able to delay treatment until clearance from COVID-19 precautions.

Discussion

At the outset of the pandemic, our clinical staff reviewed current and upcoming patients and designated them into three tiered priority levels, as previously detailed.[8] Level 1 patients were deemed the highest priority to continue therapy, including patients who had already started treatment courses, those with highly symptomatic metastatic disease, or those with rapidly progressing potentially curable cancer. The policy indicated that patients who convert to COVID-19−positive or PUI status would need to be placed on a treatment break unless there was an urgent indication for treatment. Based on the institutional policy, that treatment break duration for COVID-19 patients would at minimum be 10 to 14 days or require 2 consecutive negative tests before clearance from precautions. This policy, though certainly necessary at the time, placed a burden on the treating physician to make difficult and ultimately subjective decisions about patient care and threatened the pillars of patient autonomy and mutual decision making.

Importantly, total treatment time (TTT) can have a profound effect on oncologic outcomes. A National Cancer Database analysis of patients with head and neck cancer receiving definitive chemoradiation demonstrated that prolonged TTT (>56 days) was associated with worse overall survival (hazard ratio, 1.29).[9] In cervical cancer treated with chemoradiation, TTT beyond 56 days was associated with a 17% increase in pelvic failure.[10] Similarly, time to treatment initiation (TTI) from diagnosis has also been associated with mortality rates. In head and neck cancer, TTI beyond 2 months was associated with a 13% increased risk of death.[11] Effects of prolonged TTI on survival have also been demonstrated in disease sites considered to be more indolent on a relative scale, such as intermediate risk prostate cancer.[12]

One obvious concern that the COVID-19 pandemic posed for the radiation oncology community was the potential for patient cure to be compromised, whether it be due to COVID-19 infection necessitating a treatment break or a significant delay in treatment initiation. This problem is particularly salient when considering that the pandemic had already contributed to delayed diagnoses,[13,14] due to decreased cancer screening rates and outpatient workup accessibility. Moreover, in the palliative setting, the ability to use radiation therapy to manage symptoms such as intractable pain and bleeding can constitute the difference between a patient spending the remainder of their time alone in a hospital room (due to strict visitation rules) or being surrounded by loved ones in home hospice. The implementation of a COVID-19 biocontainment protocol helped to mitigate the effect of the pandemic on patient care within our radiation oncology network, where well-defined safety protocols and filtration systems to eliminate contaminated air before returning to the departmental circulation helped provide comfort to staff members and patients alike.

We must now acknowledge that the COVID-19 *pandemic* is transitioning to becoming *endemic*. Like many others, our radiation oncology department was forced to rapidly enact safety measures that we had hoped at the time would only be temporary. However, it is now clear that the need for biopreparedness is anything but temporary. In June 2022 alone, there were 3.1 million cases of documented COVID-19 infection and over 10,100 COVID-related deaths in the United States. This number rivals the 12,469 total number of deaths attributed to the entirety of the 2009 H1N1 influenza pandemic in the United States, according to the White House American Pandemic Preparedness report published in September 2021. There were several conclusions stated within this directive from a national perspective, including that there will be an increasing frequency of biological threats in the future and that current investment to mitigate "the toll of future pandemics . . . is an economic and moral imperative." The need to treat COVID-19 positive radiation oncology patients remains an undeniable part of our foreseeable future. The latest strains of COVID-19 dominating the current surge are the most transmissible and immune-evasive yet,[15] and with each wave comes the opportunity for selective pressures to produce new strains with unpredictable behavior and severity. In health care, the COVID-19 pandemic has taught us that approaching these situations with a reactive rather than a proactive stance may not be the best practice. Our experience sets the highest possible standard for biocontainment utilization in radiation oncology. We anticipate that this report will assist other radiation oncology clinics to understand and implement biopreparedness features for future infectious outbreaks, thereby addressing the needs of patients with cancer in the safest possible manner.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2022.101094.

References

1. Orazem M, Oblak I, Spanic T, Ratosa I. Telemedicine in radiation oncology post-COVID-19 pandemic: There is no turning back. *Int J Radiat Oncol Biol Phys*. 2020;108:411-415.
2. Elledge CR, Beriwal S, Chargari C, et al. Radiation therapy for gynecologic malignancies during the COVID-19 pandemic: International expert consensus recommendations. *Gynecol Oncol*. 2020;158:244-253.
3. Yahalom J, Dabaja BS, Ricardi U, et al. ILROG emergency guidelines for radiation therapy of hematological malignancies during the COVID-19 pandemic. *Blood*. 2020;135:1829-1832.
4. Obek C, Doganca T, Argun OB, Kural AR. Management of prostate cancer patients during COVID-19 pandemic. *Prostate Cancer Prostatic Dis*. 2020;23:398-406.
5. Sherry D, Rooney MK, Bernard V, Seo A, Marqueen KE, Schrank BR. Residency interviews in radiation oncology after COVID-19: Perspectives from recently matched applicants. *Int J Radiat Oncol Biol Phys*. 2020;108:452-454.
6. Sandhu N, Frank J, Eyben R, et al. Virtual radiation oncology clerkship during the COVID-19 pandemic and beyond. *Int J Radiat Oncol Biol Phys*. 2020;108:444-451.
7. Tang LV, Hu Y. Poor clinical outcomes for patients with cancer during the COVID-19 pandemic. *Lancet Oncol*. 2020;21:862-864.
8. Wright JL, Alcorn SR, McNutt T, et al. An integrated program in a pandemic: Johns Hopkins radiation oncology department. *Adv Radiat Oncol*. 2020;5:666-672.
9. Shaikh T, Handorf EA, Murphy CT, Mehra R, Ridge JA, Galloway TJ. The impact of radiation treatment time on survival in patients with head and neck cancer. *Int J Radiat Oncol Biol Phys*. 2016;96:967-975.
10. Song S, Rudra S, Hasselle MD, et al. The effect of treatment time in locally advanced cervical cancer in the era of concurrent chemoradiotherapy. *Cancer*. 2013;119:325-331.
11. Murphy CT, Galloway TJ, Handorf EA, et al. Survival impact of increasing time to treatment initiation for patients with head and neck cancer in the United States. *J Clin Oncol*. 2016;34:169-178.
12. Cone EB, Marchese M, Paciotti M, et al. Assessment of time-to-treatment initiation and survival in a cohort of patients with common cancers. *JAMA Netw Open*. 2020;3: e2030072.
13. Kaufman HW, Chen Z, Niles JK, Fesko YA. Changes in newly identified cancer among US patients from before COVID-19 through the first full year of the pandemic. *JAMA Netw Open*. 2021;4: e2125681.
14. Walker MJ, Wang J, Mazuryk J, et al. Delivery of cancer care in Ontario, Canada, during the first year of the COVID-19 pandemic. *JAMA Netw Open*. 2022;5: e228855.
15. Cao Y, Yisimayi A, Jian F, et al. BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection. *Nature*. 2022;608:593-602.