A Retrospective Descriptive Study of Remdesivir Treatment in the Home or Outpatient Setting Among Adult Patients Diagnosed with Coronavirus Disease 2019 (COVID-19)

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ABSTRACT

Background
At the onset of the COVID-19 pandemic, early conflicting evidence complicated implementation of therapy. Despite this dilemma, comprehensive outpatient care including integration of remdesivir treatment was scaled up in a multi-center, integrated health care system. This retrospective descriptive report describes program characteristics and learnings from the frontline.

Methods
Treatment guidelines, medical center policies, implementation checklists, and workflow diagrams were evaluated for cohesion. From a pool of eligible patients with COVID-19 enrolled in remote patient monitoring (RPM), a sub-cohort of patients 18-75 years of age who had received remdesivir between December 15, 2020 and August 31, 2022, either in tents/infusion center staffed with nurses proximate to hospitals or via home infusion was identified via prescription dispensing database.

Results
Among 21,766 patients who enrolled in a COVID-19 pandemic RPM, >95% had positive COVID-19 evaluation and 80% entered the program from the emergency room or hospital. A subset of 1,776 patients was treated with remdesivir of which 1,427 (80%) received treatment before the FDA expanded indication. Highest outpatient remdesivir quantity dispensed occurred between July 2022 and December 2022 associated with prevalence of the highly transmissible Omicron and subvariants. Average outpatient remdesivir treatment duration was 2.59 days.

Conclusions
Rapid implementation of comprehensive outpatient care of COVID-19 was facilitated by multiple factors including expeditious adoption of RPM and telehealth to support traditional home health and advanced medical care at home. While patients treated with remdesivir comprised a small percentage of all RPM patients, this critically timed option during recurrent surges helped to relieve strained hospital resources.

Keywords: COVID-19, remdesivir, home infusion, outpatient, implementation

Introduction

Early in the coronavirus disease (COVID-19) pandemic, only intravenous biologics and remdesivir (RDV) a potent antiviral, were available under Emergency Use Authorization. Subsequently in October 2020, remdesivir emerged as the first Food and Drug Administration-approved drug for treating COVID-19. Initial use was intended for a hospital or health care setting capable of providing acute care comparable to inpatient hospital care.[1-2]

Despite these developments, implementation of therapy was delayed. Among contributing factors were fluctuating evidence and authoritative treatment guidelines while already strained hospitals struggled to withstand repeated COVID-19 surges.[3-9] Against this background, patients with lower oxygenation and severe clinical status who previously would have been admitted had to be diverted to the outpatient setting.[10-12]

Concurrently, hospitals that had previously applied to participate in the Centers for Medicare & Medicaid Services "Hospital without Walls" program were galvanized to participate in the expanded initiative to include acute hospital care at home. Targeting patients who require acute inpatient admission to a hospital with daily rounding by a physician and a medical team monitoring care needs on an ongoing basis, acute care is provided by a hybrid of telehealth, remote monitoring, and regular in-person visits by nurses. It differs from traditional home health which provides skilled nursing and other skilled care services in the home.[13]

Such delivery systems of care were sporadic during COVID-19 surges resulting in limited research on implementation. This report overcomes this gap by describing program characteristics and facilitators of large-scale comprehensive outpatient care, including integration of remdesivir treatment in a multi-center, integrated health care system.

Methods

Setting

Kaiser Permanente Southern California (KPSC) is a non-profit integrated health system with 15 medical centers and provides comprehensive preventive and medical care to approximately 4.7 million members who are demographically similar to the diverse socioeconomic, ethnic California population at large.[14] Treatment guidelines, medical center policies, implementation checklists, and workflow diagrams were evaluated in a crosswalk for cohesion and COVID-19 outpatient care program components identified.

The KPSC Institutional Review Board (IRB) reviewed and approved all study activities with waiver of written informed consent. All methods were conducted in accordance with relevant guidelines and regulations in accordance with the Declaration of Helsinki. This descriptive report followed the relevant elements of the Standards for Reporting Qualitative Research guidelines for retrospective observational data.

Components

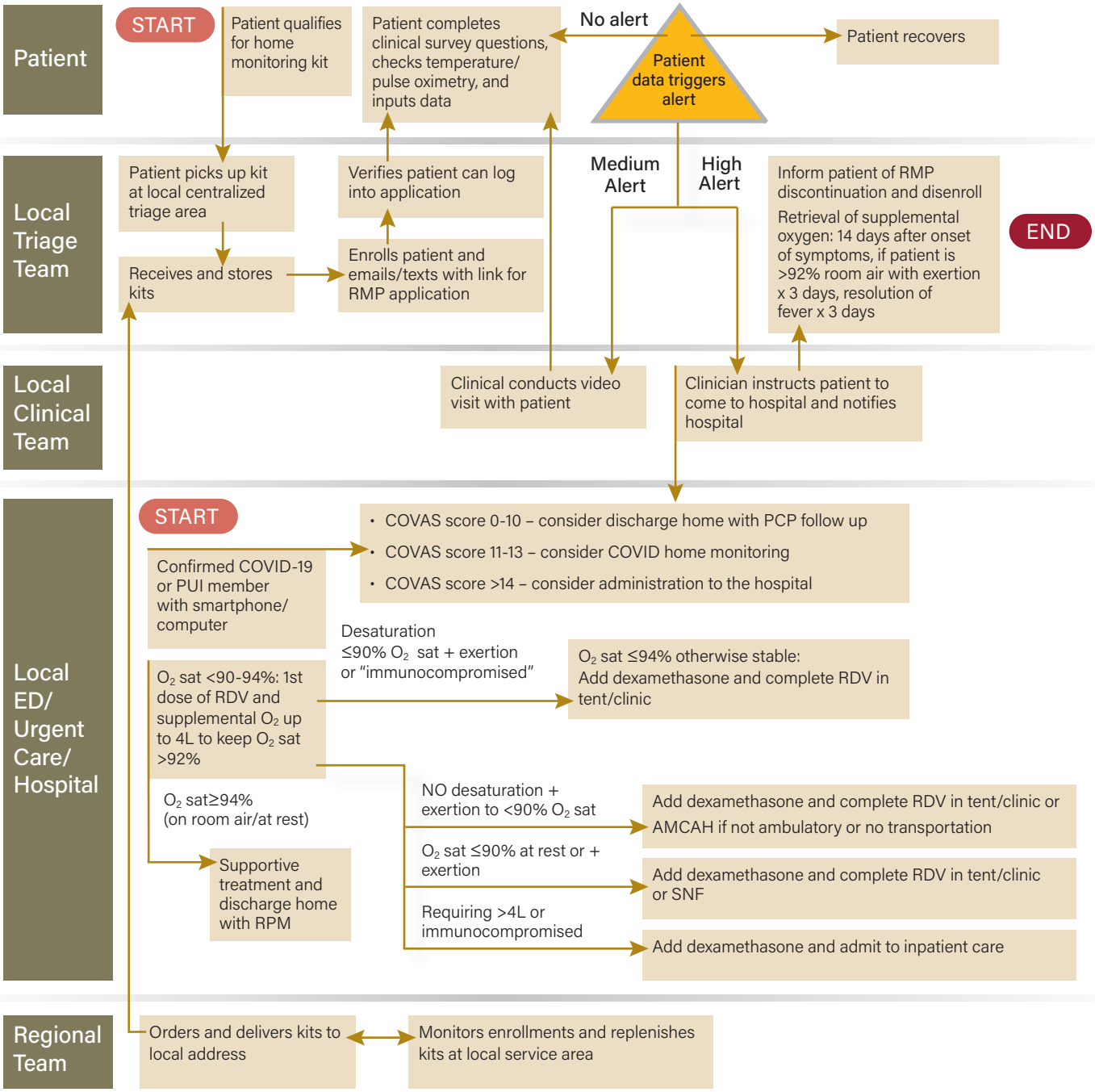
Remote patient monitoring (RPM)

The KPSC COVID-19 remote patient monitoring (RPM) initiative was launched on April 13, 2020, and completed region roll-out on August 3, 2020. The COVID-19 Outpatient Monitoring & Treatment Workflow Process is depicted in Figure 1. Participation required patients to be alert and oriented to self-report symptoms and have a smart phone/computer.

Patients enrolled in RPM were sent home with a remote monitoring kit that included a thermometer, pulse oximeter, and a software platform that enabled video capability and daily patient surveys. Patient education initiated in the hospital or emergency room was reinforced by the home visiting nurse. Patients were notified to take daily up to every 8-hour measurements including temperature, oxygen saturation, and to complete a symptom check survey. Links to up-to-date COVID-19 information and meditation/relaxation application were also included. RPM oversight was provided by clinical support teams of local providers, virtual medical center, or on-call continuing care physicians. Redeployed providers including social workers, pharmacists, physical, and respiratory therapists were engaged to support lab and vital signs monitoring.

If patient measurements were out of range for defined parameters, medium to high alerts were sent to clinicians. A medium alert was generated for oxygen reading <92% or 3% lower than previous entry, which prompted a physician video visit. A high alert was generated for oxygen saturation reading <90% or 4% lower than previous entry, and patients were automatically alerted to seek immediate medical attention. High alerts also prompted physicians to arrange for hospital admission.

FIGURE 1 | Covid-19 Outpatient Monitoring & Treatment Workflow Process



All enrolled RPM patients were visible to clinicians within their medical center through a COVID-19 clinical dashboard in the electronic medical record. On-demand, live reports through the vendor platform could be generated by both the regional command center and local administrators, providing useful metrics on:

- Total volumes
- Enrollments
- Patient adherence
- Patient satisfaction
- Length of stay
- Patient end points
- Home oxygen orders
- COVID status for persons under investigation
- Demographics
- Patient entry points
- Task response time
- Alert volumes
- Times

Disenrollment from RPM occurred when one of the following criteria was met: 14 days since symptom onset, 3 days since last fever, or 3 days of respiratory improvement. Early detection of patient deterioration expedited hospital admission or treatment with medications. A detailed description of the KPSC RPM initiative and preliminary results have been previously reported.[15]

Risk Assessment

Initial eligibility criteria for RPM enrollment were health system members with confirmed COVID-19 or person under investigation (PUI) identified in the emergency room, urgent care, or hospital setting with oxygen saturation >92%, heart rate <100 bpm, respiratory rate <20 breaths/min, mild symptoms, low disease burden, age <60 years, and body mass index <40. These criteria were later replaced in May 2020 by a validated predictive COVID risk score, COVAS, which assessed comorbidities, obesity/BMI ≥40, vital signs, age, and sex for patient risk stratification.[16]

Depending upon entry point, patients from the emergency room or urgent care were stratified into 3 risk categories based on COVAS score.

- For COVAS score of 0-10, discharge home with primary care provider with follow up was recommended.
- For those with a COVAS score of 11-13, enrollment in RPM was recommended.
- For COVAS score >14, hospitalization was considered.

Patients discharged from the hospital were further risk stratified based on required supplemental oxygen 2-5 L/min.

Remdesivir Treatment

Remdesivir infusions required COVID-19 baseline laboratory results to be available prior to administration. All first doses were administered in a controlled setting and continuous monitoring for adverse drug events was performed.

Linkage with the medical center allowed the home infusion pharmacy to procure remdesivir during initial shortages for outpatient reallocation while it was still indicated for acute use. Initial 5-day treatment with remdesivir 200 mg loading dose on the first day and 100 mg daily for 4 additional days was the standard regimen. This outpatient regimen was later updated to an early 3-day course of remdesivir validated by a recent study, where an early 3-day course of remdesivir among non-hospitalized patients who were at elevated risk for COVID-19 progression demonstrated benefit with significant risk reduction of COVID-19-related hospitalizations and all-cause death.[17]

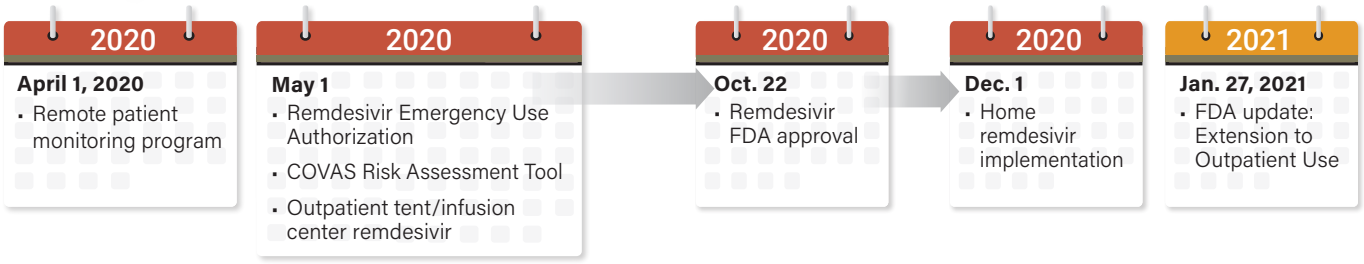
Outpatient/Home Infusion

Pulse oximetry oxygen saturation (SpO_2) ≥94% on room air with symptoms and SpO_2 <94% on room air and/or requiring low–flow supplemental oxygen (<6 L/minute) was used as the threshold value for primary triage stratification. To be eligible for home health, symptomatic patients with SpO_2 <90% had to be medically stable during observation in the ER or hospital. If symptoms had not progressed in 24 hours, they were treated similarly to symptomatic patients with SpO_2 90-94% who were otherwise stable. After the first dose of remdesivir administration was confirmed, they were enrolled in RPM and referred for home infusion to complete the regimen.

Nurses initiated a virtual video follow-up visit with the physician while at the home for the next day infusion of remdesivir and daily as needed. Patients could be discharged from home health or AMCAH after completion of remdesivir and continue with the RPM until disenrollment.

Daily or every other day labs included complete blood cell count with differential, basic metabolic panel, liver function tests, and protime/INR that were obtained by an external contracted independent phlebotomy

FIGURE 2 | Timeline of Remdesivir Use



provider group. Daily point of care test glucose monitoring for patients with diabetes or elevated daily glucose while on a corticosteroid was considered on a case-by-case basis for patients without diabetes.

Early remdesivir discontinuation was considered for adverse effects: ALT 5-10 times the upper limit of normal with signs of liver inflammation occurring by the third day of remdesivir. Escalation to re-hospitalization was considered for patients with worsening prognosis, increasing oxygen requirement, confusion, and critical laboratory results.

Telehealth

Simultaneous integration of multiple technology vendors and point product applications were utilized to streamline care coordination and transform the patient telehealth experience. They encompassed live video, asynchronous patient data sharing, and mobile health applications. A hallmark feature was real-time, HIPAA-compliant secure communication to expand access to providers in the field and remotely. Additional features included linkage to the electronic medical record care management workbench to transmit instantaneous information, 24/7 back to the care team, and a billing mechanism for Medicare and Medicaid reimbursements. Virtual physician follow-up was available 7 days a week and after hours.

Results

RPM was implemented at 12 of 15 medical centers by August 3, 2020. Among 21,766 patients who enrolled in COVID-19 pandemic RPM, all completed by meeting disenrollment criteria. More than 95% tested positive for COVID-19 and 80% entered from the emergency room or hospital. Enrollment duration in RPM was 11 days (mean) ranging 1-14 days with high adherence to daily monitoring of temperature, oxygen saturation, and symptoms (92%). Approximately 11% were hospitalized while enrolled in RPM. Figure 2 depicts timeline of outpatient care.

Local virtual clinical teams supporting RPM ranged in size from 7 to 165 and were comprised of nurses (171) and physicians from the hospital, emergency room, and urgent care (219). Other specialties supporting this core team were internal medicine/family medicine (12), and geriatrics/continuing care/emeritus (53). A total of 284 physicians not including rotation physician coverage were trained. Volume of COVID-19 patients by medical center who completed RPM ranged from 298 to 4,237. Traditional home health agencies performed monitoring for 2,316 patients until discontinuation of the RPM initiative on May 2, 2022. An additional 181 COVID-19 patients were monitored by the AMCAH model until August 31, 2022, for a total of 2,497 patients.

A subset of 1,776 patients was treated with remdesivir of which 1,427 (80%) received treatment before the FDA expanded indication on January 27, 2022 for outpatient treatment of mild-moderate COVID-19 and at elevated risk for progression to severe COVID-19, including hospitalization or death. The majority of patients (93%, n=1,659) was referred by 3 of 5 medical centers which implemented outpatient remdesivir treatment. Infectious disease physicians were actively involved with planning and implementation at 2 medical centers. Average outpatient treatment duration was 2.59 days. Highest outpatient remdesivir utilization occurred between July and December 2022 associated with prevalence of the highly transmissible SARS-CoV-2 variant Omicron and subvariants.

Discussion

This report retrospectively describes multiple seamless facilitators of outpatient COVID-19 care including expeditious adoption of an RPM initiative leveraging

diverse health care workers that allowed detection of patients in early stages of deterioration. Use of the COVAS risk score efficiently standardized stratification of patients who would most benefit from treatment intervention with critically timed remdesivir during surges. Telehealth further allowed scaling up while reducing COVID-19 exposure for other patients and health care workers.[18] These findings support similar previously reported strategies to increase acute health service capacity.[19-21]

Limitations

The descriptive design of this report did not evaluate remdesivir treatment effectiveness or value of outcomes to patients, providers, and health care organizations.[22-23] One such outcome is provider and patient satisfaction with massive technology upgrades to enable RPM and telehealth with the trade-off in lack of a single interface and end-user application in one universal platform. Furthermore, we did not assess why some medical centers opted to participate in AMCAH vs traditional home health and outpatient remdesivir and others did not.

Scaling up of this care model would be incomplete without mention of treatment cost, a potential barrier to integration of outpatient remdesivir. The Institute for Clinical and Economic Review (ICER) preliminary cost recovery pricing for a 10-day course of remdesivir was estimated at $10. An estimated ceiling of $4,500 threshold for cost-effectiveness pricing was used for treatment of large patient populations.[24] Until Medicare Part B updated its reimbursement policy, inability to link billable telehealth services with outpatient remdesivir and its administration limited generalizability to a fee-for-service setting. In an updated ICER report, a health-benefit price benchmark of $2,470 for hospitalized patients with moderate-to-severe disease and $70 for patients hospitalized with milder disease was used to reflect less severely ill patients.[25]

Conclusion

RPM and telehealth that maintained standard of care, privacy, and real-time patient data exchange buttressed the framework for delivery of care in the home. While patients treated with remdesivir comprised a small percentage of all RPM patients, this critically timed option during recurrent surges relieved strained hospital resources by enabling early discharges or avoiding admission. These findings demonstrate the feasibility of an expanded comprehensive outpatient care model and provide learnings for future application to a large-scale emergency response.

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