Effectiveness of a On-site Medicalization Program for Nursing Homes With COVID-19 Outbreaks

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Received: June 24, 2020; Editorial Decision Date: July 29, 2020

Decision Editor: Anne B. Newman, MD, MPH

Abstract

Background: Nursing homes are highly vulnerable to the occurrence of COVID-19 outbreaks, which result in high lethality rates. Most of them are not prepared to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic.

Method: A coordinated on-site medicalization program (MP) in response to a sizeable COVID-19 outbreak in 4 nursing homes was organized, with the objectives of improving survival, offering humanistic palliative care to residents in their natural environment, and reducing hospital referrals. Ten key processes and interventions were established (provision of informatics infrastructure, medical equipment, and human resources, universal testing, separation of “clean” and “contaminated” areas, epidemiological surveys, and unified protocols stratifying for active or palliative care approach, among others). Main outcomes were a composite endpoint of survival or optimal palliative care (SOPC), survival, and referral to hospital.

Results: Two hundred and seventy-two of 457 (59.5%) residents and 85 of 320 (26.5%) staff members were affected. The SOPC, survival, and referrals to hospital occurred in 77%, 72.5%, and 29% of patients diagnosed before the start of MP, with respect to 97%, 83.7%, and 17% of those diagnosed during the program, respectively. The SOPC was independently associated to MP (OR = 15 [3–81]); and survival in patients stratified to active approach, to the use of any antiviral treatment (OR = 28 [5–160]). All outbreaks were controlled in 39 [37–42] days.

Conclusions: A coordinated on-site MP of nursing homes with COVID-19 outbreaks achieved a higher SOPC rate, and a reduction in referrals to hospital, thus ensuring rigorous but also humanistic and gentle care to residents.

Keywords: Community-based long-term care, COVID-19, Frailty, Multimorbidities, SARS-CoV-2
facilities, the impact of COVID-19 on human health by affecting the most vulnerable population, and therefore conditioning the subsequent health care system saturation, is a real danger that can be devastating (11,12). Data are scarce, but affected nursing home populations may be a significant proportion of all COVID-19 cases in some countries (11–13). Another consequence of this fact is the potential transmission to community, and hence, the persistence of SARS-CoV-2 circulation. As a matter of fact, nursing homes are integrated in the community, and their facilities are opened to residents’ families, friends, and different community resources. Unfortunately, most of them lack structure and work flows to face an epidemic of this magnitude; many of them are poorly connected with the health care system, count with lower staff ratio (adjusted to attend “stable” residents), and have suboptimal staff training and expertise in managing patients with COVID-19 (11–13). Therefore, many COVID-19 outbreaks affecting nursing home residents, staff members, and residents’ families have occurred (14–16).

In the present work, we detail an innovative coordinated on-site medicalization program (MP), which was carried out in response to a sizeable COVID-19 outbreak declared in last days of March 2020, in 4 nursing homes of Seville province (Southern Spain, 1 942 389 inhabitants, 688 592 of them living in the city) with the aim of offering medically rigorous but also humanistic care to residents with COVID-19 in their natural environment, avoiding the community widespread of SARS-CoV-2 thorough specific and forthright measures, and minimizing hospital saturation, helping therefore to achieve a better and proper use of these resources. Specifically, we will describe all details of the MP and its achievements in terms of survival or optimal palliation of treated residents, as well as hospital referral reductions.

Patients and Methods

On March 17, 2020, a 98-year-old patient coming from a nursing home was admitted to Hospital Universitario Virgen del Rocío (tertiary teaching center of Seville with a reference population of 557 576 citizens) and diagnosed with COVID-19. The following days, up to 27 new cases coming from the same nursing home and other 3 similar facilities located in the city of Seville, within the hospital's reference area, were also transferred and diagnosed with the disease. Under these circumstances, a Primary Care and Hospital-coordinated MP was quickly built. This program contained informatics, medical equipment and material, pharmacy, and human resources to fully attend the outbreaks in the 4 nursing homes on-site. The MP was initiated between 1st and 6th April, 2020 in all these residential centers.

Reference Population and Inclusion Criteria

The total population was 777 people, 457 of them were residents (86 years old [Quartile 1–Quartile 3 (Q–Q3) = 79–91], 75% women), and 320 were staff-members. A description of the magnitude of the outbreak is detailed in Table 1. All residents diagnosed with COVID-19 were included in the MP. All staff members were treated and followed up with the hospital current management protocols, but were excluded from the present study.

Medicalization Program Characterization

The program contained the following critical processes and interventions carried out on-site in all 4 nursing homes:

1. Locating a “clean room” for informatics equipment, clinical work, consulting and writing in electronic clinical charts, and administrative tasks. Full connection with health care electronic information systems.
2. Locating a secure locker room for health care workers’ dressing and undressing. Ensuring personal protective equipment supplies to all MP team members.
3. Universal SARS-CoV-2 testing to residents and staff members. Real-time polymerase chain reaction (RT–PCR) for the detection of specific viral RNA from nasopharyngeal swab-smears, and lateral flow serologic method from fingerstick blood samples for the detection of specific antibodies against SARS-CoV-2 were performed. For these purposes, the Allplex 2019-nCoV RT-PCR assay (Seegene Inc., Seoul, South Corea), for detection of gene targets ORF1ab and N; the VIASURE SARS-CoV-2 RT-PCR assay (CerTest Biotec S.L., Zaragoza, Spain), for detection of gene targets RdRP, E, and N; and the Wondfo SARS-CoV-2 Antibody Test Lateral Flow Method assay (Guanzhou Wondfo Biotech Co Ltd, Guangzhou, China), for the detection of IgM and IgG antibodies, were implemented. We performed both methods at once in order to accelerate decision making and to avoid acute infection confirmations delay.

SARS-CoV-2 acute infection was defined either as the detection of viral ribonucleic acid by RT–PCR (“positive nasopharyngeal swab PCR”), as the presence of IgM or IgG antibodies (“positive serology”), or both.

4. Establishment of a “clean area” with rooms and common spaces to which uninfected residents were moved, and a “contaminated area” with rooms and common spaces to which residents with confirmed infection were moved. Warrant the compulsory use of personal protective equipment to all members of the work team while remaining in the contaminated area.

Table 1. Global Data of the 4 Nursing Homes’ COVID-19 Outbreaks in the City of Seville, Spain

| Nursing Home | Number of Residents | Age of Residents | Gender, Female | Date of Outbreak Start | Number of Affected Residents | Number of Affected Staff Members | Number of Deaths in Affected Residents |
|--------------|---------------------|------------------|----------------|------------------------|-----------------------------|----------------------------------|---------------------------------------|
| NH1          | 168                 | 86 [81–92]       | 126 (75%)      | March 17, 2020         | 123 (73%)                  | 44 (35.2%)                       | 29 (25%)                             |
| NH2          | 155                 | 85 [78–89]       | 114 (73.5%)    | March 23, 2020         | 93 (60%)                    | 21 (19.3%)                       | 23 (24.7%)                           |
| NH3          | 101                 | 88 [81–92]       | 85 (81%)       | March 25, 2020         | 35 (35.6%)                  | 11 (17.7%)                       | 6 (16.7%)                           |
| NH4          | 33                  | 86 [79–90]       | 23 (70%)       | March 26, 2020         | 21 (63.6%)                  | 9 (37.7%)                        | 3 (14.2%)                            |
| Total        | 457                 | 86 [79–91]       | 348 (75%)      | March 17–26, 2020      | 272 (59.5%)                 | 85 (26.5%)                       | 61 (22.4%)                           |

Notes: NH = nursing home.

* Median [Quartile 1–Quartile 3]. † With respect to all residents. ‡ All of them with mild-moderate symptoms or asymptomatic. § With respect to all staff members.

| With respect to all affected with COVID19 (lethality).
5. Specific training of staff members in the management and care of COVID-19 patients. Separation of those working in the clean area and those working in the contaminated area, with prohibition to change shifts between professionals from these 2 areas. Proper clinical attention and quarantine of staff members with confirmed SARS-CoV-2 acute infection until obtaining a negative nasopharyngeal swab PCR (they were tested weekly, counting from the first day without symptoms).

6. Meticulous epidemiological survey and follow-up to trace the outbreaks’ origin and evolution.

7. Electronic admission of all residents with demonstrated SARS-CoV-2 infection, which allowed electronic health records’ checking, writing, ordering blood extractions, and drug prescribing as if patients were in-hospital.

8. Enough provision of equipments, expendables, and drugs: material for blood extractions, intraintravenous and subcutaneous lines, intraintravenous fluids, oxygen therapy, electrocardiographs, a portable ultrasound, and hospital medications (antiviral agents, intraintravenous drugs, etc.) among others.

9. Provision of health care workers (physicians and nurses), covering clinical attention 24 hours during 7 days in the week. They were mixed teams with Primary Care (Family and Community Medicine), Hospital (Internal Medicine), and Emergency (Emergency Medicine) professionals. A reckoning of 60 health care workers were mobilized (35 physicians and 25 nurses).

10. Elaboration of a common clinical management and treatment algorithm, and a common communication protocol to daily inform families by phone about the clinical status of both affected and not affected residents.

Clinical Algorithm and Treatment Protocols

The main clinical algorithm is detailed in Figure 1. After a thorough clinical evaluation, based on the 6-month adapted “surprise question” (“would I be surprised if this patient dies in the next six months?”), patients’ and families’ preferences, and after consulting patient’s advance directives for life-support, all residents with COVID-19 were offered either active standard care or advanced palliative care.

All patients were daily assessed for early mobilization, sitting and starting physical therapy. Clinical cure was defined after 3 days of being asymptomatic, and microbiological cure when the patient tested a control negative nasopharyngeal swab PCR after clinical cure. All patients were isolated in the “contaminated area” for 14 days after being asymptomatic; then, were performed a control nasopharyngeal swab PCR before discharging and transferring them to the “clean area.”

Active standard care

Patients in this group were actively treated with hydroxychloroquine (HCQ) with or without lopinavir/ritonavir (LPV/RTV) (under judgment of clinician in charge) with the addition of adjuvant and antimicrobial treatments in the circumstances detailed in Supplementary Table S1. Daily measurement of vital signs, clinical follow-up until 3 days after being asymptomatic, and at least during the whole antiviral treatment were carried out. Blood sample extraction to assess biological parameters was available. Point-of-care ultrasonography (POCUS) (VsScan Extend Dual Probe, GE Healthcare, Little Chalfont, UK) was performed if oxygen saturation fell below 94% or 5 or more points from patient’s baseline saturation. Any clinical, biological, or ultrasound data of macrophage activation syndrome-like disease were monitored to implement first-line anti-inflammatory treatment.

Advanced palliative care

All patients in this group were offered a single room, ensuring comfort, personalized care, and spiritual support. A global multidimensional evaluation was performed with symptomatic focus and medications were daily adjusted. Oxygen therapy and antimicrobials were used when dyspnea/hypoxemia or bacterial co-infection were present, respectively. In some patients, corticosteroids were also used, but never before the fifth day of symptoms beginning. Clinicians were proactively aware of end-of-life/agony symptoms and signs occurrence; in this situation, palliative sedation as well as the accomplishment of one family member were offered; the accompanying family member was offered a personal protective equipment with specific instructions on its use. An optimal palliative care was defined when the complete process (offering, acceptance, and materialization of all the above mentioned issues, including the offering of palliative sedation and accomplishment if indicated) was accomplished.

Treatment protocols included antiviral treatment, adjuvant treatments, and antimicrobials are detailed in Supplementary Table S1.

Follow-up, Referrals, and Discharge

All patients were followed-up according to the previously detailed clinical algorithm. For the purposes of this study, a 30-day period after SARS-CoV-2 infection confirmation was established. When clinically indicated (Figure 1), referrals to hospital were organized and programmed with the clinicians attending in-hospital COVID-19 patients. Patients who met previously detailed clinical and microbiological criteria of cure were discharged and moved to the clean area.

Demedicalization Criteria

After 14 days of the last confirmed COVID-19 case, the nursing home was eligible for demedicalization. In this process, the following requirements were ensured:

1. A contingency plan with infection and prevention measures, active surveillance, actions in case of new infections, and provision of spaces and rooms for possible future “contaminated areas.”
2. Urgent notification of the appearance of suspected cases compatible with COVID-19.
3. Continuous training to staff members.
4. Staff members control through daily temperature measurement and a responsible declaration at the entrance to the workplace of not having symptoms compatible with COVID-19, and in case of symptoms onset, urgent notification.
5. Public and auditable weekly check-list of the infection control measures.

Data Collection and Variables
A complete set of demographical, clinical, functional, and pharmacological data were retrospectively collected from all the cohort of included patients. Clinical data included the different diseases, and all possible comorbidities, previous medications, functional parameters by means of Barthel's index, prognostic parameters by means of PROFUND indexes, different symptoms and signs, medical treatments, and outcome (17,18). These data were collected by clinicians in charge, who were active members of the investigation team.

The main outcome was a composite variable, which was accomplished if SOPC of residents with COVID-19 occurred. For this purpose, we looked at survival as dichotomous, so subjects were categorized depending on whether they survived COVID-19 or not after the follow-up period. An optimal palliative care was defined as detailed previously.

Secondary outcomes were survival in those patients stratified to active standard care, number of patients who needed to be referred to hospital, and the mean number of hospital referrals per week. For this purpose, we looked at survival as both a dichotomous and as time-dependent outcome. For the dichotomous outcome, subjects were categorized depending on whether or not they survived COVID-19 after the follow-up period. For the continuous outcome, survival time was defined as the number of days between the symptoms onset date (diagnosis date in those patients with asymptomatic infection) and the date of death.

At last, we evaluated the daily number of community-acquired new COVID-19 cases, as well as the total cumulative incidence of citizens living in Seville city during the same time period, in order to empirically establish possible relations between both epidemic curves.

Statistical Analysis
The dichotomous variables were described as whole integers and percentages, and the continuous variables as mean and standard deviation (or median and interquartile range in those with no criteria of normal distribution). The distribution of all variables was analyzed with the Kolmogorov–Smirnov test. Possible differences in SOPC, survival, patients needing hospital referral, and hospital referral rates per week were firstly investigated performing the chi-squared test (with the Yates correction and, when necessary, the Fisher exact test), the Student's t for normally distributed quantitative variables, and Mann–Whitney U test in the case of quantitative variables that were not normally distributed.

We included the factors which showed statistical differences in unadjusted analysis, in a multivariable backward stepwise logistic regression model in order to obtain those independently associated to SOPC. With respect to survival in patients stratified to receive active standard care, we also included the factors which showed statistical differences in unadjusted analysis, in a multivariable Cox proportional hazards model for time to death, in order to obtain those independently associated to survival. In this group of patients, we also performed Kaplan–Meier curves (and log-rank test), considering death as a time-dependent variable, to assess differences in survival trajectories of those diagnosed before or during the implementation of the MP.

The strength of associations was quantified by calculating odds ratio (OR) using 95% confidence intervals. Statistic analysis was performed by M.B.-W. using the SPSS 22.0 software.

Ethical Aspects
All patients or their legal representatives accepted the use of their anonymous clinical data for clinical research purposes. The study was approved by the local ethics committee (internal code 1199-N-20). In this retrospective project, the collection, process, and analysis of all data were anonymously carried out, and only for the purposes of the project. All data were protected in accordance with the European Union directive 2016/679 of the European Parliament and the European Council, of April 27, 2016, regarding the protection of persons and their personal data.

Results
In total, 357 people of 777 (46%) were infected by SARS-CoV-2; of them 272 of 457 (59.5%) were residents, and 85 of 320 (26.5%) were staff members (Table 1). The median number of days since first resident was diagnosed with COVID-19 until the start of MP were 12 [11–14], and the median duration of MP was 39 [37–41] days. The main differential clinical and biological features of all residents affected are detailed in Table 2. Briefly, they were mostly aged women, with multiple chronic conditions, functional decline, and polypharmacy. The most frequent symptoms were fatigue and global deterioration, followed by low-grade fever, dyspnea, cough, anorexia, diarrhea, and delirium. Sixty-six residents (24%) developed no symptoms or mild symptoms. All staff members developed mild-to-moderate symptoms or stayed asymptomatic.

Residents affected were diagnosed with a positive nasopharyngeal swab PCR test (229 [84.2%]), rapid serological test (21 [7.7%]), or both (22 [8.1%]). After the initial evaluation, 189 (69.5%) were proposed for active standard care and 83 (30.5%) for advanced palliative care. The most frequent interventions were oxygen therapy (114 patients, 42%), intravenous lines and fluids (86, 32%), parenteral drugs (intravenous or intramuscular; 64, 23.5%), POCUS (50 procedures, 18.4%), and transfusions (2 patients). In those proposed for active standard care, according to established protocols (Supplementary Table S1), antiviral treatment was administered to 139 (73.5%) patients; the most frequent scheme was HCQ (114 patients, 60%) followed by HCQ plus LPV/RTV (18, 10%), and HCQ plus azithromycin (7, 5%). Low-molecular-weight heparin was administered to 119 patients (44%), antimicrobials to 62 (23%), and systemic corticosteroids to 57 (21%).

All patients proposed for advanced palliative care were treated with supportive care. Additionally, they were treated with low-molecular-weight heparin (36, 43%), antimicrobials (33, 39.8%), antiviral drugs (30, 36%), and corticosteroids (21, 25%).

The most frequent complications and main outcomes are detailed in Table 3. A 13% (n = 24) and a 45% (n = 37) of patients proposed for active standard or for optimal palliative care died, respectively. In multivariate analysis, the main outcome SOPC was independently associated to COVID-19 diagnostic confirmation during MP (OR = 15
In those patients stratified to receive active standard care, survival rates were 82% before MP and 96% during MP \((p = .004, \text{OR} = 3.4 [1.2–10])\). In this group, survival time was independently associated to the absence of dyspnea \((\text{OR} = 16 [5–50], p < .001)\), or fatigue-general deterioration at presentation \((\text{OR} = 5 [1.7–14], p < .001)\); a lower PROFUND index score \((\text{OR} = 1.17 [1.05–1.3], p = .004)\); lower serum C-reactive protein \((\text{OR} = 1.009 [1.004–1.015], p = .001)\), and ferritin levels \((\text{OR} = 1.001 [1–1.001], p = .01)\); and the use of any antiviral treatment \((\text{OR} = 28 [5–160], p < .001)\). The differential time-dependent survival in this group of residents diagnosed with COVID-19 before the start or during MP is detailed in Figure 2.

### Table 2. Main Clinical Features of Residents With COVID-19 During 4 Nursing Homes Outbreaks in Seville, Spain

| Clinical Features | Global \((N = 272)\) | Patients Diagnosed With COVID-19 Before MP \((N = 149)\) | Patients Diagnosed With COVID-19 During MP \((N = 123)\) |
|-------------------|----------------------|------------------------|------------------------|
| Mean (SD)/Median [Q1–Q3]/No. (%) | | | |
| Age and female gender | 87 [81–91]; 205 (75.4%) | 88 [83–91]; 108 (72.5%) | 86 [79–90]; 97 (79%) |
| No. of comorbidities per patient | 4 [3–6] | 4 [3–6] | 4 [3–6] |
| Most frequent comorbidities | | | |
| Hypertension | 198 (73%) | 116 (78%) | 82 (67%) \((p = .04)\) |
| Dyslipidemia | 104 (38.2%) | 57 (38.3%) | 47 (38.2%) |
| Advanced dementia | 103 (37.8%) | 55 (37%) | 48 (39%) |
| Osteoarthritis | 76 (28%) | 42 (28%) | 34 (27.6%) |
| Depression | 72 (26.5%) | 40 (27%) | 32 (26%) |
| Diabetes mellitus | 71 (26%) | 40 (27%) | 31 (25%) |
| Mild–moderate dementia | 64 (23.5%) | 37 (25%) | 27 (22%) |
| NL disease with severe impairment | 59 (22%) | 25 (17%) | 34 (27.6%) \((p = .03)\) |
| Cerebrovascular disease | 53 (19.5%) | 27 (18%) | 26 (21%) |
| Atrial fibrillation | 52 (19%) | 33 (22%) | 19 (15%) |
| Chronic heart failure | 38 (14%) | 20 (13%) | 18 (15%) |
| Anxiety disorders | 37 (13.6%) | 19 (14%) | 23 (19%) \((p = .03)\) |
| COPD or asthma | 36 (13%) | 22 (15%) | 14 (12%) |
| Coronary artery disease | 34 (12.5%) | 19 (15%) | 5 (4%) \((p < .001)\) |
| Parkinson disease | 30 (11%) | 17 (14%) | 13 (10.6%) |
| Hypothyroidism | 24 (8.8%) | 13 (8.7%) | 11 (9%) |
| Basal Barthel’s Index | 49.5 (30) | 47 (29) | 52 (31) |
| PROFUND index | 8.2 (4) | 8.5 (4) | 7.7 (3.3) |
| No. of chronic prescribed drugs/patients with extreme polypharmacy (>10 drugs) | 7.2 (3.6) / 50 (18.4%) | 7.1 (4.29) (19.5%) | 7.4 (3.5)/21 (17%) |
| Most frequent symptoms | | | |
| Fatigue and global deterioration | 105 (38.6%) | 63 (42%) | 42 (34%) |
| Low-grade fever \((37–37.9°C)\) | 98 (36%) | 63 (42%) | 35 (28.5%) \((p = .04)\) |
| Dyspnea | 102 (37.5%) | 74 (50%) | 28 (23%) \((p < .001)\) |
| Cough | 94 (34.6%) | 53 (36%) | 41 (33.3%) |
| Anorexia | 55 (20%) | 27 (18%) | 28 (23%) |
| Diarrhea | 52 (19%) | 26 (17.5%) | 26 (21%) |
| Delirium | 47 (17.3%) | 29 (19.5%) | 18 (15%) |
| High-grade fever \((≥38°C)\) | 45 (16.5%) | 25 (17%) | 20 (16%) |
| Nausea/vomiting | 17 (6.3%) / 16 (5.9%) | 13 (8.5%) / 11 (7%) | 4 (3.3%) /5 (4%) |
| Sneezing–runny nose | 10 (3.7%) | 9 (6%) | 1 (0.8%) \((p = .023)\) |
| Fall(s) | 7 (2.6%) | 4 (2.7%) | 3 (2.4%) |
| Ageusia/anosmia | 4 (1.5%) / 3 (1.1%) | 2 (1.3%) / 2 (1.3%) | 2 (1.6%) /1 (0.8%) |
| Main biological parameters | | | |
| Hemoglobin (g/dL) | 11.7 (2.3) | 11.8 (2.1) | 11.7 (2.4) |
| Leukocytes \((\times 10^9)\) | 7862 (3903) | 8910 (4300) | 7021 (3300) \((p = .008)\) |
| Lymphocytes \((\times 10^9)\) | 1262 (667) | 1353 (666) | 1150 (657) |
| Platelets \((\times 10^9)\) | 249 000 (114 000) | 245 000 (126 000) | 252 000 (105 000) |
| D dimer | 2231 (3932) | 2529 (5000) | 1990 (2800) |
| Creatinine (mg/dL) | 1.34 (1.3) | 1.49 (1.3) | 1.21 (1.3) |
| ASAT | 29 (26) | 34 (31) | 25 (31) |
| ALAT | 23 (24) | 29 (31) | 19 (14) \((p = .03)\) |
| Creatinine kinase | 144 (412) | 174 (295) | 121 (484) |
| PCR | 70 (97) | 94 (94) | 50 (95) \((p = .012)\) |
| Ferritin (ng/mL) | 456 (464) | 660 (867) | 307 (357) \((p = .009)\) |

Note: ALAT = alanine aminotransferase; ASAT = aspartate aminotransferase; COPD = chronic obstructive pulmonary disease; MP = medicalization program; NL = neurological; Q1–Q3 = Quartile 1–Quartile 3. Bold values refer to those with significant differences in patients diagnosed before vs during MP. Significance threshold was .05.
In the epidemiologic survey, it was stated that in all nursing homes, the symptom onset dates of the first affected staff members preceded in 5.5 (Q1–Q3 = 2–9.7) days to those symptom onset dates of the first affected residents (Supplementary Figure S1). The global outbreak dynamics are reflected in Supplementary Figure S2. The peak of residents with active infections was reached on April 13th (175 patients), and after this date, we observed a progressive fall of these, together with a rise in the number of recovered patients, as well as a stabilization and absence of new cases. The first nursing home fulfilling demedicalization criteria reached them on May 12, 2020, and the last one on May 14th. Globally, the 4 outbreaks’ median duration was 50 [49–54] days after their start. At the time of writing of this article, no new cases had been diagnosed and since April 30, 2020, all surviving residents remained without any COVID-19 symptoms. The last microbiologically cured resident was a 99-year-old woman whose control nasopharyngeal swab PCR tested negative on May 21, 2020. Addressing the same periods of the 3 preceding years, a noteworthy peak in the number of deceased residents was observed in the 4 nursing homes, as detailed in Supplementary Figure S3.

The peak of new community-acquired COVID-19 in Seville city was reached on March 25, 2020 with 87 new cases. Afterwards, a progressive decline of daily new cases was observed, and nowadays its transmission is residual (Supplementary Figure S4). Globally, in this first pandemic wave, 1094 COVID-19 cases (cumulative incidence 158.8 cases/100 000 inhabitants) have been diagnosed in the city of Seville, 32.4% of them occurred in the nursing home outbreaks, summing up affected residents and staff members living in the city. None of the 60 health care workers taking part in the MP was infected.

**Discussion**

The incorporation of a coordinated MP in the management and control of 4 sizeable COVID-19 outbreaks in nursing homes resulted in significant better outcomes of the composite endpoint of survival or optimal end-of-life care (SOPC), as well as reductions in hospital referral rates. This MP virtuously gathered substantial hospital and primary care resources as well as internal medicine, primary care, and epidemiology professionals during an intense but short time period.

Specifically, the reduction of COVID-19 mortality during MP to nearly 16% was notably lower if compared to other reported outbreaks in long-term care facilities (27%–33%) (11,14,15), and also when compared to rates of in-patients of our hospital (54% in those older than 80 years, data not published) or to patients of same ages in Spain (globally 22%, and 48.5% in those needing hospital care) (2). The MP also achieved as additional benefits, the development of

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**Table 3. Unadjusted Differential Complications and Outcomes of Affected Residents During the Medicalization Program of 4 Nursing Homes With COVID-19 Outbreaks in Seville, Spain**

| Parameter, Mean (SD)/Median [Q1–Q3/N (%)] | Patients Diagnosed With COVID-19 Before MP (N = 149) | Patients Diagnosed With COVID-19 During MP (N = 123) |
|------------------------------------------|-----------------------------------------------------|--------------------------------------------------|
| Patients with complications 127 (47%) 83 (56%) 44 (36%), p = .001 [0.4; 0.3–0.7] | 44 (36%), p = .001 [0.4; 0.3–0.7] |
| Acute respiratory failure 106 (39%) 74 (50%) 32 (26%), p < .001 [0.3; 0.2–0.6] | 32 (26%), p < .001 [0.3; 0.2–0.6] |
| Persistent or incidental delirium 36 (13%) 21 (14%) 15 (12%) | 15 (12%) |
| Immobility and “bedridden syndrome” 32 (12%) 20 (13.7%) 12 (10%) | 12 (10%) |
| LRT bacterial infections 28 (10.3%) 14 (10%) 14 (11.5%) | 14 (11.5%) |
| Acute renal failure 19 (7%) 13 (9%) 6 (5%) | 6 (5%) |
| Oropharyngeal dysphagia 16 (6%) 10 (7%) 6 (5%) | 6 (5%) |
| Urinary tract infection 15 (5.5%) 8 (5.5%) 7 (5.7%) | 7 (5.7%) |
| Pressure ulcers 14 (5.1%) 9 (6%) 5 (4%) | 5 (4%) |
| Number of complications per patient 1.04(1.5) 1.25 (1.6) 0.8 (1.3), p = .02 | 0.8 (1.3), p = .02 |

CI = confidence interval; LRT = low respiratory tract; MP = medicalization program; OR = odds ratio; Q1–Q3 = Quartile 1–Quartile 3. Bold values refer to those with significant differences in patients diagnosed before vs during MP. Significance threshold was .05.

*aComposite endpoint of survival or optimal end-of-life care.*
fewer medical complications, and a more comfortable and peaceful care process in those with a previous poor life expectancy.

We think that the clues to explain the benefits of MP are three: First, it enabled an earlier symptom recognition by well-trained professionals, which led to earlier treatments and support measures; this is an evident fact common to all diseases; in this sense, our data show that stratifying and treating very old patients with potentially acceptable life expectancy are safe and of probable benefit; otherwise we could fall in a somehow nihilist deviation of clinical practice (19–21). Second, it allowed the on-site care in the natural environment of patients, which led to fewer complications, mainly due to less geriatric syndrome occurrence; early mobilization, rehabilitation, and use of common spaces and rooms in the contaminated area for the continuity of activities prevented the highly frequent complications of hospital care; as a matter of fact, rooms of hospital wards dedicated to COVID-19 are isolated, and interactions with patients generally restricted to the strictly necessary (19). Third, it incorporated humanistic and gentle attention to the most frail and terminally ill residents, enabling a personalized care according to preferences of patients and families; the rush of a pandemic situation should not make palliative care invisible, on the contrary, an exquisite stratification and subsequent optimal palliative care has to be offered to this selected population in order to avoid futile and unnecessary iatrogenic interventions (20, 21); in this sense, it is important to remark that optimal palliative care does not mean death; as a matter of fact, 55% of patients stratified to optimal palliative care survived COVID-19.

Epidemiological surveys showed that SARS-CoV-2 could have entered nursing homes either by staff members or by visitors in preceding days to the declaration of national alarm state by the Government of Spain on March 14, 2020 (22). Then, the virus spread fast, probably because of the same reasons as those already detailed in similar outbreaks (14,15,23). The city epidemic curve ran parallel but preceded a few days those observed in the nursing homes outbreaks, which supports the previously commented hypothesis. No impact of the delayed incidental case peak of nursing homes outbreaks was observed in the global epidemic curve of the city; nevertheless we can extract no definitive conclusions because this could reflect the absence of transmission from nursing homes to community due to the MP, the effects of national lockdown measures, or both.

One of the leading results of this study is the complete clinical picture of COVID-19, that we obtained in a large sample of frail older people. We observed the typical patterns of COVID-19 less frequently, whereas more subtle and unspecific symptoms and presentations were more prevalent. This has also been observed by other authors and follows the pattern of getting sick in geriatric populations, which is well known with respect to other diseases (24,25). Of notable remark is the absence of prognostic influence of any comorbidities taken them individually; only their combination in the PROFUND index showed prognostic ability. In contrast, some COVID-19 symptoms and biological parameters, such as dyspnea, fatigue and general deterioration, C-reactive protein, and ferritin levels, showed a strong independent association with death. The presence of any of these symptoms in old patients with COVID-19 has to put us on alert.

Another remarkable finding was the strong independent association of antiviral treatments with survival. This fact is both concordant as well as contradictory to previous reports and puts in the front line the urgent needs of counting with evidence to optimally treat COVID-19 patients (26–31). In the absence of this evidence, we are of the opinion that best available choices (those safest drugs with best previous results) should be offered to patients. In this sense, we opted to use HCQ with or without LPV/RTV, because of their extensive use in many protocols (29,30).

The MP was a huge effort on many levels, but the effectiveness shown proved this effort to be worth it. Many voices and societies have emphasized that nursing homes and other long-term care facilities are the most vulnerable environments to the effects of SARS-CoV-2 pandemic (11), urging all actors (community leaders, governments, health and social care authorities) to prioritize them in their strategies (32–34). In some countries like Spain, this fact is even more critical due to its high life expectancy and the significant number of older citizens living in these facilities (35). But beyond statements and guidelines, reality also needs pragmatic actions and interventions, because these extraordinary times need our help with unprecedented solutions (36).

The main lessons we have learned after the MP task are also 3: First of all, we learned that nursing homes are key elements and one of the main targets in the fight against possible future SARS-CoV-2 pandemic waves; many have considered them in the border of health care and social services, and because of that their connections and boundaries to both systems are somehow imprecise, as many countries have painfully witnessed; it is time to globally rethink the role and place of nursing homes in our societies, and to really work in a deeper integration of health and social care (11,23,33). Second, we learned that health care resources re-allocation is an effective strategy to manage this pandemic, and that decisive and anticipated actions save lives and prevent unfortunate consequences; one may think that this mobilization was exaggerated and expensive, but otherwise at least 200 of these residents would have needed hospital care, so in this scenario, the same health care resources would have been used, but in a overcrowded and saturated hospital. And at last we learned that a true synergistic coordination between Primary and Hospital Care is possible and it works. We all have read a lot about this issue, and know, however, the daily difficulties in its implementation (37). In these extraordinary circumstances, integration worked wonderfully, because it emerged from professionalism values: willingness to serve people, altruism, generosity, and mutual respect.

This study has some limitations that should be remarked. First, the retrospective collection of the cohort’s data could have introduced some biases, as it is already known for this kind of approach. Second, the confidence intervals for some of the findings are wide, reflecting limits in study power for some analyses. And third, the possible regression to the mean, which is present in most health care initiatives directed towards high-risk populations, could have played a role in the results; however, we think that this effect is not at all present in the obtained data, because when MP started, obviously all patients (included those who were diagnosed previously) were attended; so, these last patients also received the benefits of the program, but were treated in the analysis of endpoints as if they had not.

In conclusion, our work show that a coordinated on-site MP of nursing homes with COVID-19 outbreaks achieved better outcomes of survival and optimal palliative care, as well as a reduction in referrals to hospital, thus ensuring rigorous but also humanistic and gentle care to residents.

Supplementary Material

Supplementary data are available at The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences online.
Funding
None declared.

Conflict of Interest
None declared.

Acknowledgments
Our support and affection to all residents, their families, and the nursing homes’ staff members for their collaboration, patience, and resilience. Special thanks to all members of Primary Care and Hospital COVID teams listed below, and health managers who have worked so hard to heal and alleviate patients and their families.

Manuel Molina and Rosario Amaya (Manager and Medical Director of Hospital Universitario Virgen del Rocio); José M. León-Sotelo and Susana Padrones (Manager and Medical Director of Primary Care District of Seville); Verónica Alfaro, Concepción Alonso, Amagoya Pérez, Bosco Barón, Remedios Biempica, Trinidad Cano, Encarna Escudero, Fátima Espinosa, Rosa Gámiz, Rocio González, Aurora González, Sonia Gutierrez, Carlos Hernandez, Rocio Hidalgo, Joaquín García, Carlos Jiménez, Eusebio Jiménez, Juan C. Jiménez, Julia Lanseros, Francisca León, Carmina López, Rosario Martínez, Rocio Paramio, María C. Pulido, Antonio Rodriguez, Santiago Rodriguez, Rosa Ruiz, Victor Sánchez, and Josefa Vega (Internal Medicine and Vascular Surgery Departments, Hospital Universitario Virgen del Rocio); Laura Acosta, Alberto Adrada, Claudia Bernabeu, Juan J. Blanco, Maite Brea, Manuela Camps, Ángela Cejudo, Yolanda Corchado, Víctor Cuéberos, Laura Escudero, Alba Espada, Miguel Florencio, Ana García, María J García, Miriam García, Alejandra Gomez, Raúl M. Gómez, Francisco J. González, Manuela Gutierrez, Margarita Gutierrez, Jose L. Hernández, Jaime Huertas, Isabel León, Alba Lozano, María E. Lucio-Villegas, Cristina Márquez, Carmen Martínez, Patricia Medina, Ana M. Moral, Alba Morales, Alejandra Morilla, María M. Muñoz, Jesús Neri, Carlos Máiquez, María Martínez, Patricia Medina, Ana M. Moral, Jose M. Murillo, Pablo Quiro, Raúmundo Rivas, Aurora Rodríguez, Sara Rodríguez, María Roma, María A. Ruiz, María J. Sánchez, Miguel F. Sayago, María Sumariva, Diego L. Toledo, Antonio Trigos, Carmen Tous, and Cristina Villañà (Primary Care District of Seville); Eduardo Briones, Bárbara Díaz, María Ruiz, and Rocío Sillero (Epidemiology and Public Health Department, Primary Care District of Seville); Javier Bautista, Sandra Flores, Antonio Monzón, and Bernardino Santos (Pharmacy Department, Hospital Universitario Virgen del Rocio); Mariola Carballo, Juan C. Domingo, Ingrid Ferrer, Juan F. Gil, Teresa Molina, and Daniel Palma (Pharmacy Department, Primary Care District of Seville); Manuela Aguilar, José M. Cisneros, Elisa Cordero, Nuria Espinosa, Manuel Garcia, Marta Herrero, José M. Lomas, Rafael Laque, José Molina, María D. Navarro, María Pamagia, Manuel Poyatos, Julia Prenza, Cristina Rocca, and César Sotomayor (Infectious Diseases Department, Hospital Universitario Virgen del Rocio); Cristina Anadeo, Enrique Calderón, Antonio Domínguez, Emilio García, Álvaro López, Isabel López, Aurora Morillo, Esther Pérez, Rafaela Ríos, Jesús F. Rodríguez, Sonia Sánchez, and Javier Toral (Emergency Department, Hospital Universitario Virgen del Rocio); Teresa Aldabó, Rafael Bellido, Jesús Carbajal, Manuel Casado, Manuela Cid, Yael Corcia, Javier Corona, Alicia Cuadra Calabrhoa, Diego X. Cuenca, Ana Diaz, Reginal Deusseck, Sara Escalon, Ana Escorces, Carmen Ferrandiz, Ignacio Gallego, Joso Gaspar, María L. Gascón, Horacio García, Carmen Gómez, Inmaculada Herrera, Mercedes Jiménez, Antonio Marín, Sara Martín, Luis Martin, María Mendoza, Álvaro Pastor, José Pérez, and Zaida Ruiz de Azna (Intensive Care Department, Hospital Universitario Virgen del Rocio); Mariibel Asensio, Candela Caballero, Michelle Espinosa, Marta Ferrer, Demetrio González, and Luis Jara (Pneumology Department, Hospital Universitario Virgen del Rocio); Almudena Aguilera, Amelia Rodriguez, and Nieves Romero (Cardiology Department, Hospital Universitario Virgen del Rocio); Carmen Grande and Alejandro Suárez (Nephrology Department, Hospital Universitario Virgen del Rocio); and Javier Ampuero and Teresa Ferrer (Gastroenterology Department, Hospital Universitario Virgen del Rocio).

References
1. European Centre for Disease Prevention and Control. COVID-19 situation update for the EU/EEA and the UK, as of 25 May 2020. Accessed May 26, 2020. https://www.ecdc.europa.eu/en/cases-2019-n cov-eueea
2. Instituto de Salud Carlos III Report on the situation of COVID-19 in Spain. Report COVID-19 n° 32. May 21, 2020. Accessed May 26, 2020. https:// www.isciii.es/QueHacemos/Servicios/VigilanciaSaludPublica/RENAVE/ EnfermedadesTransmisibles/Paginas/InformesCOVID-19.aspx
3. Anonymous. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep, 2020;69:343–346. doi:10.15585/mmwr. mm6912e2
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054–1062. doi:10.1016/S0140-6736(20)30566-3
5. Bonafè M, Prattichizzo F, Giuliani A, Storci G, Sabbatinelli J, Olivieri F. Inflamm-aging: why older men are the most susceptible to SARS-CoV-2 complicated outcomes. Cytokine Growth Factor Rev. 2020;53:33–37. doi:10.1016/j.cytofgre.2020.04.005
6. Graselli B, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response [published online ahead of print March 13, 2020]. J Am Med Assoc. doi:10.1001/jama.2020.4031
7. Steinberg E, Balakrishna A, Habboushe J, Shawl A, Lee J. Calculated decisions: COVID-19 calculators during extreme resource-limited situations. Emerg Med Pract. 2020;22(Suppl. 4):CD1–CD5.
8. Petersen A, Largent EA, Karlawish J. Ethics of reallocating ventilators in the COVID-19 pandemic. BMJ. 2020; 369:m1828. doi:10.1136/bmj.m1828
9. Rosenbaum L. Facing COVID-19 in Italy—ethics, logistics, and therapeutics on the Epidemic’s Front Line. N Engl J Med. 2020;382:1873–1875. doi:10.1056/NEJMp2004942
10. Mannelli C. Whose life to save? Scarce resources allocation in the COVID-19 outbreak. J Med Ethics. 2020;46:364–366. doi:10.1136/medethics-2020-106227
11. Fallon A, Dukelow T, Kennelly SP, O’Neill D. COVID-19 in nursing homes. QJM. 2020;113:391–392. doi:10.1093/qjmed/hca136
12. Tseng TG, Wu HL, Ku HC, Tai CJ. The impact of the COVID-19 pandemic on disabled and hospice home care patients [published online ahead of print April 3, 2020]. J Gerontol A Biol Sci Med Sci. 2020;75(9):e128–e129. doi:10.1093/gerona/glaa081
13. Quigley DD, Dick A, Agarwal M, Jones KM, Mody L, Stone PW. COVID-19 preparedness in nursing homes in the midst of the pandemic. J Am Geriatr Soc. 2020;68:1164–1166. doi:10.1111/jgs.16520
14. Tan LF, Seetharaman SK. COVID-19 outbreak in nursing homes in Singapore [published online ahead of print May 13, 2020]. J Microbiol Immun Infect. doi:10.1016/j.jmii.2020.04.018
15. McMichael TM, Currie DW, Clark S, et al.; Public Health–Seattle and King County, Washington. Team. Epidemiology of Covid-19 in a long-term care facility in King County, Washington [published online ahead of print April 3, 2020]. J Microbiol Immun Infect. doi:10.1016/j.jmii.2020.04.018
16. Kwiatkowski M, Nadonly TL. At least 2,300 nursing homes have coronavirus cases—and the reality is likely much worse. USA Today, April 13, 2020.
17. Bernabeu-Wittel M, Ollero-Baturone M, Moreno-Gaviño I, et al. Development of a new predictive model for polypathological patients. The PROFUND index. Eur J Intern Med. 2011;22:311–317. doi:10.1016/j.ejim.2010.11.012
18. Mahoney FJ, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J. 1965;14:61–65.
19. Lauretani F, Ravazzoni G, Roberti M, et al. Assessment and treatment of older individuals with COVID 19 multi-system disease: clinical and ethical implications. Acta Biomed. 2020;91:130–168. doi:10.23750/abm.v91i2.5629

Downloaded from https://academic.oup.com/biomedgerontology/article/76/3/e19/5879759 by guest on 22 July 2021
20. Kunz R, Minder M. COVID-19 pandemic: palliative care for elderly and frail patients at home and in residential and nursing homes. Swiss Med Wkly. 2020;150:w20235. doi:10.4414/smw.2020.20235

21. Borasio GD, Gamondi C, Obrist M, Jox R; for the Covid-Task Force of Palliative Ch. COVID-19: decision making and palliative care. Swiss Med Wkly. 2020;150:w20233. doi:10.4414/smw.2020.20233

22. Government of Spain. Royal Decree 463/2020, of March 14, declaring the state of alarm for the management of the health crisis situation caused by COVID-19. Official State Bulletin Nº 67, March 14, 2020. Accessed May 26, 2020. https://www.boe.es/eli/es/rd/2020/03/14/463/con

23. Rada AG. Covid-19: the precarious position of Spain’s nursing homes. Br Med J. 2020;369:m1554. doi:10.1136/bmj.m1554

24. Tay HS, Harwood R. Atypical presentation of COVID-19 in a frail older person. Age Ageing. 2020;49:525–524. doi:10.1093/ageing/aaz1068

25. Ward CF, Figiel GS, McDonald WM. Altered mental status as a novel initial clinical presentation for COVID-19 infection in the elderly. Am J Geriatr Psychiatry. 2020;28:808–811. doi:10.1016/j.jagp.2020.05.013

26. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. Br Med J. 2020;369:m1849. doi:10.1136/bmj.m1849

27. Ye XT, Luo YL, Xia SC, et al. Clinical efficacy of lopinavir/ritonavir in the treatment of coronavirus disease 2019. Eur Rev Med Pharmacol Sci. 2020;24:3390–3396. doi:10.26355/eurrev_202003_20706

28. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. N Engl J Med. 2020;382:1787–1799. doi:10.1056/NEJMoa2001282

29. Martinez MA. Compounds with therapeutic potential against novel respiratory 2019 coronavirus. Antimicrob Agents Chemother. 2020;64. doi:10.1128/AAC.00399-20

30. Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19. N Engl J Med. 2020;382:2411–2418. doi:10.1056/NEJMoa2012410

31. Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med. 2020;288:192–206. doi:10.1111/joim.13091

32. American Geriatrics Society. American Geriatrics Society Policy Brief: COVID-19 and nursing homes. J Am Geriatr Soc. 2020; 68:908–911. doi:10.1111/jgs.16477

33. Davidson PM, Szanton SL. Nursing homes and COVID-19: we can and should do better. J Clin Nurs. 2020; 29:2758–2759. doi:10.1111/jocn.15297

34. Lloyd-Sherlock PG, Kalache A, McKee M, Derbyshe J, Geffen L, Casas FG. WHO must prioritise the needs of older people in its response to the Covid-19 pandemic. Br Med J. 2020;368:m1164. doi:10.1136/bmj.m1164

35. Pérez-Díaz J, Abellán-García A, Aceituno-Nieto P, Ramiro-Fariñas D. A profile of the elderly in Spain, 2020. Basic statistical indicators. In Informes Envejecimiento en red nº 25. Madrid (CSIC) 2020. Accessed May 26, 2020. http://envejecimiento.csic.es/documentos/documentos/entred-indicadoresbasicos2020.pdf

36. Gaur S, Dumyati G, Nace DA, Jump RLP. Unprecedented solutions for extraordinary times: helping long-term care settings deal with the COVID-19 pandemic. Infect Control Hosp Epidemiol. 2020;41:729–730. doi:10.1017/ice.2020.98

37. Sadler E, Potterton V, Anderson R, et al. Service user, carer and provider perspectives on integrated care for older people with frailty, and factors perceived to facilitate and hinder implementation: a systematic review and narrative synthesis. PLoS ONE. 2019;14:e0216488. doi:10.1371/journal.pone.0216488