4 (17%) did not tolerate PP for more than 1 hour, 5 (21%) tolerated it for 1 to 3 hours, and 15 (63%) tolerated it for more than 3 hours. Characteristics of the patients and main results are displayed in the Table. The median time from admission to first PP was 1 day (interquartile range, 0-1.5 days). Neither sedation nor anxiolytics were used.

Six patients were responders to PP, representing 25% (95% CI, 12%-45%) of the 24 patients included and representing 40% (6/15) (95% CI, 20%-64%) of the patients who sustained PP for 3 hours or more. Three patients were persistent responders. Among patients who sustained PP for 3 hours or more, PaO₂ increased from a mean of 73.6 (SD, 15.9) mm Hg before PP to 94.9 (SD, 28.3) mm Hg during PP (difference, 21.3 [95% CI, 6.3-36.3] mm Hg; P = .006) (Figure). No significant difference was found between PaO₂ before PP and PaO₂ after resupination (P = .53).

None of the included patients experienced major complications. Back pain was reported by 10 patients (42%) during PP. At the end of a 10-day follow-up period, 5 patients required intubation. Four of them did not sustain PP for 1 hour or more and required intubation within 72 hours.

Discussion | In this study of patients with COVID-19 and hypoxemic respiratory failure managed outside the ICU, 63% were able to tolerate PP for more than 3 hours. However, oxygenation increased during PP in only 25% and was not sustained in half of those after resupination. These results are consistent with findings from previous small studies of PP in non-intubated patients. Back pain was reported by 10 patients (42%) during PP. At the end of a 10-day follow-up period, 5 patients required intubation. Four of them did not sustain PP for 1 hour or more and required intubation within 72 hours.

Further studies to identify optional PP regimens and patients with COVID-19 in whom it may be beneficial are warranted.

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Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit

The pandemic of coronavirus disease 2019 (COVID-19), with a large number of patients requiring respiratory support, threatens to overload intensive care units (ICUs). Noninvasive ventilation (NIV) use in general wards may be an alternative for some patients but has seldom been described and is not used worldwide.1 One study described the feasibility of NIV in the prone position2; pronation can recruit dorsal lung regions and drain airway secretions, improving gas exchange and survival in acute respiratory distress syndrome (ARDS).3 We report respiratory parameters after using this intervention in a case series of patients with COVID-19.

Methods | On April 2, 2020, in San Raffaele Scientific Institute, Milan, Italy, COVID-19 patients with ARDS were treated either in the ICUs (n = 48) or medical wards (n = 202).

Noninvasive ventilation was used for 62 patients with mild to moderate respiratory distress syndrome. The median time from admission to first prone position was 3 hours (interquartile range, 1-7.5 hours). The median time from admission to first NIV was 3 hours (interquartile range, 1-6.5 hours). The median time from admission to first prone position was 3 hours (interquartile range, 1-7.5 hours).

Letters
On April 2, 2020, we performed a cross-sectional survey to identify all patients undergoing the prone position NIV outside the ICU, irrespective of the day they started using this technique. Respiratory parameters were measured at 3 time points: before NIV, during NIV in pronation (60 minutes after start), and 60 minutes after NIV end. We investigated oxygen saturation as measured by pulse oximetry (SpO2), derived PaO2:FIO2, respiratory rate, and patient’s comfort using a numerical rating scale (0, totally uncomfortable, to 10, fully comfortable). Follow-up was conducted at 14 days to determine how many patients were discharged, were still treated in the prone position, or were intubated. Continuous measures were compared using Wilcoxon matched pairs signed rank test or t test if paired data were normally distributed. Two-sided \( P < 0.05 \) defined statistical significance. All analyses were performed with STATA version 16 (STATA Corp). The study was approved by the Ethics Committee of IRCCS San Raffaele Scientific Institute. Written informed consent was obtained.

**Results** | Fifteen patients receiving NIV in the prone position outside the ICU on April 2 were identified. Mean (SD) age was 59 years (6 years); 13 were men. Noninvasive ventilation in the prone position started a median of 5 days (interquartile range [IQR], 3-10 days) before April 2 (Table) and no patient started NIV in the prone position on April 2. The median number of NIV cycles in the prone position on April 2 was 2 (IQR, 1-3 cycles) for a total duration of 3 hours (IQR, 1-6 hours). Compared with baseline, all patients had a reduction in respiratory rate during and after pronation (\( P < .001 \) for both) (Figure); all patients had an improvement in SpO2 and PaO2:FIO2 during pronation (\( P < .001 \) for both); 12 patients (80%) had an improvement in SpO2 and PaO2:FIO2 after pronation; 2 (13.3%) had the same value; and 1 (6.7%) had worsened. Compared with baseline, 11 patients (73.3%) had an improvement in comfort during pronation and 4 (26.7%) had the same value; 13 patients (86.7%) had an improvement in comfort after pronation and 2 (13.3%) had the same

### Table. Baseline Characteristics of 15 Patients With COVID-19 Who Received Noninvasive Ventilation in the Prone Position Outside the ICU

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>59 (6.5)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>24 (3.4)</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Men</td>
<td>13 (86.6)</td>
</tr>
<tr>
<td>Time, median (IQR), d</td>
<td></td>
</tr>
<tr>
<td>From first symptom appearance</td>
<td>15 (12-21)</td>
</tr>
<tr>
<td>From hospitalization</td>
<td>9 (7.5-14)</td>
</tr>
<tr>
<td>From NIV start</td>
<td>7 (4-10)</td>
</tr>
<tr>
<td>From NIV in the prone position start</td>
<td>5 (3-10)</td>
</tr>
<tr>
<td>PaO2:FIO2 on first MET call*</td>
<td>157 (43.0)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; COVID-19, coronavirus disease 2019; FIO2, fraction of inspired oxygen; ICU, intensive care unit; IQR, interquartile range; MET, medical emergency team; NIV, noninvasive ventilation; PaO2, arterial partial pressure of oxygen.

*The normal PaO2:FIO2 ratio is more than 400 mm Hg; a PaO2:FIO2 of less than 300 mm Hg indicates acute respiratory distress syndrome.

**Figure. Respiratory Parameters in the Individual Patients Before, During, and After Noninvasive Ventilation in the Prone Position**

The graphs represent trends of respiratory parameters in the individual patient at the 3 time points. Before pronation: immediately before initiating noninvasive ventilation (NIV) while the patient was still in the supine position. During pronation: after 1 hour of receiving NIV treatment while the patient was in the prone position. After pronation: 1 hour after NIV treatment stopped when the patient was in the supine position. A, Peripheral oxygen saturation (SpO2).
value. At the 14-day follow-up, 9 patients were discharged home, 1 improved and stopped pronation, 3 continued pronation, 1 patient was intubated and admitted to ICU, and 1 patient died.

**Discussion** | Providing NIV in the prone position to patients with COVID-19 and ARDS on the general wards in 1 hospital in Italy was feasible. The respiratory rate was lower and the oxygenation was higher during and after pronation than they were at baseline. Whether intubation was avoided or delayed remains to be determined.

Limitations include the small number of patients, short duration of NIV in the prone position, and lack of a control group. Comparisons of NIV in the prone position with oxygen by face mask or NIV in the standard position are needed. Importantly, selection bias is possible. Patients were not included if NIV failed while in the prone position or were treated and either died or recovered before April 2. Therefore, patients in the study may not be representative of all patients treated with NIV in the prone position.

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**Correction:** This article was corrected online May 26, 2020, to replace the first name with the surname of one of the authors in the Author Contribution section and to identify that it was an intensive care physician who suggested assessing noninvasive ventilation in the prone position.

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**SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adults**

Confirmed cases of coronavirus disease 2019 (COVID-19) and case-fatality rates vary among countries. One reason could be national policies regarding childhood BCG vaccination, with fewer confirmed cases and a lower death toll reported in countries with vs without universal BCG vaccine coverage.1,2 Comparing outbreak characteristics between countries is influenced by potential confounders such as different phases of outbreak, mean age of affected population, management of the pandemic, amount of tests being administered, definitions of COVID-19-related deaths, or underreporting.

The BCG vaccine was routinely administered to all newborns in Israel as part of the national immunization program between 1955 and 1982. Overall, the vaccine acceptance rate in Israel is high, with greater than 90% coverage. Since 1982, the vaccine has been administered only to immigrants from countries with high prevalence of tuberculosis. This change allowed comparison of infection rates and proportions with severe COVID-19 disease in 2 similar populations with differing BCG status: individuals born during the 3 years before and 3 years after cessation of the universal BCG vaccine program.

**Methods** | The current policy of the Israeli Ministry of Health is to test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in every patient with symptoms that could be compatible with COVID-19 (cough, dyspnea, fever). Nasopharyngeal swabs were tested by real-time reverse transcriptase–polymerase chain reaction in approved laboratories between March 1 and April 5, 2020. Only 1 test per patient was included. Results were stratified by birth year. Population data for specific birth years were obtained from the national Central Bureau of Statistics. χ2 Tests were used to compare proportions and rates per 100 000 population of positive test results among persons with symptoms compatible with COVID-19 born from 1979 to 1981 (aged 39-41 years) with those born from 1983 to 1985 (aged 35-37 years). A 2-sided significance threshold was set at P < .05. The study was deemed exempt by the Shamir Medical Center institutional review board as all data were deidentified. Statistical analyses were performed using R software, version 3.5.3 (R Foundation).