**COVID-19 treatment disparities**

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**Model.**

For any risk group *k*, we can express the number of adverse COVID-related events *E* (*e.g.*, hospitalizations or deaths) in terms of the number of COVID-19 cases *C* and the number of treatments *T*  with the following equation:

Here, P(*E*|*C*) is the probability that the event *E* occurs given a symptomatic COVID-19 case *C*, and *σ* is the treatment effectiveness (*i.e.*, the proportion reduction in risk due to treatment). In plain words, this equation says that the number of adverse events *E* is equal to (a) the number of untreated COVID-19 cases times the baseline probability that the event occurs given a case, plus (b) the number of treated COVID cases times the treatment-adjusted probability that the event occurs given a case.

However, we know that we don’t observe all the cases, so we need to adjust this for imperfect ascertainment. Let *ck* (lowercase) denote the observed number of cases and *ak* denote the ascertainment rate, so that

Thus, we can re-write the first equation as

We can also simplify the equation:

If we assume that we observe all treatments *T* and all adverse events *E*, we are left with two key unknowns:

* *ak*, the case ascertainment rate. This may vary across risk groups *k.*
* *σ*, the treatment efficacy. We will assume that this is constant across risk groups, though we can relax this assumption if needed.

If we make informed guesses about these values, it is possible to calculate P(*Ek*| *ck*, *ak*) (the risk of adverse outcomes) from the available data. Furthermore, with a slight adjustment to the main equation, we can also estimate the number of adverse events that would have occurred with a different number of treatments:

Here, is the alternate number of treatments in group *k* and is the expected number of adverse events that would have occurred with treatments.

We consider two alternative ways of distributing treatments:

1. Treat every group at the same per-case rate as the group that received the most treatment.
2. Re-allocate treatments across groups in proportion to the estimated baseline (non-treatment) risk of adverse outcomes, so that the total number of treatments given is the same as the actual number of treatments given, but each risk group instead receives a share of those treatments in proportion to their baseline risk of adverse outcomes (hospitalization or death).

For the following, we will consider treatment with Paxlovid and molnupiravir separately. The analysis can be updated to reflect any of the available treatments. We assumed a 40% reduction in the risk of hospitalization and a 70% reduction in mortality risk (<https://www.acpjournals.org/doi/full/10.7326/M22-2141>).

**Results.**

Treatment re-allocation could have yielded substantially reduced hospitalizations and mortality. Treating each risk group at the same per-case rate as the most highly treated risk group (risk group 1, 31% of cases) could have averted ~5,000 hospitalizations and deaths (**Figure 1 A,C,** 50% ascertainment). Re-allocating the treatments according to baseline risk could have had an even larger impact, averting ~6,000 hospitalizations and ~12,000 deaths (**Figure 1 B,D,** 50% ascertainment). The greatest reductions in hospitalizations and mortality would have been achieved in the highest risk group (group 5) across all scenarios, for a total 2% reduction in hospitalizations and 3% reduction in mortality beyond the actual rates. For the treatment re-allocation strategy, the lowest risk groups may have had slightly higher rates of hospitalizations and mortality, but these would be offset by major reductions in hospitalizations and mortality in the highest risk groups. (**Figure 1 B,D**).These reductions reflect a roughly 5% decrease in hospitalizations and 10% decrease in mortality relative to the observed rates (**Figure 1 F,H**). Re-allocating treatments among racial-ethnic groups yields qualitatively similar, though less pronounced, results (**Figure 2**). Similar findings, though of smaller magnitude, hold for risk-based reallocation of molnupiravir (**Figure 3**).

Diagram

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**Figure 1. Raw and percent reduction in adverse events (hospitalizations, mortality) that could have been achieved through better allocation of nirmatrelvir treatment across risk groups.** (A-D) Raw estimated reduction in hospitalizations (A,B) and mortality (C,D) by adjusting the treatment rates of all risk groups to the treatment rate of the most highly treated group (A,C) and by re-allocating the treatments to the various risk groups proportionally to their raw risk of adverse outcome, keeping the total number of treatments the same (B,D). (E-H) Percent estimated reduction in hospitalizations (E,F) and mortality (G,H), relative to the observed number of hospitalizations/mortality, by adjusting the treatment rates of all risk groups to the treatment rate of the most highly-treated group (E,G) and by re-allocating the treatments to the various risk groups proportionally to their raw risk of adverse outcome, keeping the total number of treatments the same (F,H). Each plot is depicted as a function of case ascertainment rate, where low ascertainment indicates many unobserved, untreated infections and thus a smaller impact from treatment re-allocation. Colors indicate risk groups, with the black dashed line indicating the overall estimate for total (percent) reduction in adverse events.

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**Figure 2. Raw and percent reduction in adverse events (hospitalizations, mortality) that could have been achieved through better allocation of nirmatrelvir treatment across race/ethnicity groups.** (A-D) Raw estimated reduction in hospitalizations (A,B) and mortality (C,D) by adjusting the treatment rates of all race/ethnicity groups to the treatment rate of the most highly treated group (A,C) and by re-allocating the treatments to the various race/ethnicity groups proportionally to their raw risk of adverse outcome, keeping the total number of treatments the same (B,D). (E-H) Percent estimated reduction in hospitalizations (E,F) and mortality (G,H), relative to the observed number of hospitalizations/mortality, by adjusting the treatment rates of all race/ethnicity groups to the treatment rate of the most highly-treated group (E,G) and by re-allocating the treatments to the various race/ethnicity groups proportionally to their raw risk of adverse outcome, keeping the total number of treatments the same (F,H). Each plot is depicted as a function of case ascertainment rate, where low ascertainment indicates many unobserved, untreated infections and thus a smaller impact from treatment re-allocation. Colors indicate race/ethnicity groups, with the black dashed line indicating the overall estimate for total (percent) reduction in adverse events.



**Figure 3. Raw and percent reduction in adverse events (hospitalizations, mortality) that could have been achieved through better allocation of molnupiravir treatment across race/ethnicity groups.** (A-D) Raw estimated reduction in hospitalizations (A,B) and mortality (C,D) by adjusting the treatment rates of all race/ethnicity groups to the treatment rate of the most highly treated group (A,C) and by re-allocating the treatments to the various race/ethnicity groups proportionally to their raw risk of adverse outcome, keeping the total number of treatments the same (B,D). (E-H) Percent estimated reduction in hospitalizations (E,F) and mortality (G,H), relative to the observed number of hospitalizations/mortality, by adjusting the treatment rates of all race/ethnicity groups to the treatment rate of the most highly-treated group (E,G) and by re-allocating the treatments to the various race/ethnicity groups proportionally to their raw risk of adverse outcome, keeping the total number of treatments the same (F,H). Each plot is depicted as a function of case ascertainment rate, where low ascertainment indicates many unobserved, untreated infections and thus a smaller impact from treatment re-allocation. Colors indicate race/ethnicity groups, with the black dashed line indicating the overall estimate for total (percent) reduction in adverse events.