C Nicodemus **Post Covid Considerations** Spring 2023

The Covid pandemic blends into the background of viral disease burden here in 2023 but will remain endemic and continue to evolve along with the myriad of respiratory viruses we have always known. The development of immunity has reduced the risk of severe outcome for this disease and the actionable intervention that truly saved the day was the rapid development of effective vaccines using RNA technology.

I leave the chronological record of my musings on this subject posted in reverse chronological order for the historical record and for consideration by interested observers. Since the success of the RNA vaccine was not guaranteed, the exercise to reliably screen for disease protective interventions amongst commonly available medications remains a societal strategy that may once again be needed in the face of the next pandemic with yet another previously nonpathogenic micro-organism.

I continue to advise the utility of establishing a framework by which primary clinics and triage tents could evaluate hypothetically helpful treatment strategies prospectively as part of a simple and sanctioned community research network that was pre-established in the event it might be needed. In retrospect interventions that were avoided based on opinion would have proved useful, for example use of corticosteroid in the face of emerging respiratory symptoms. Some useful therapies for the Covid-19 likely were never appreciated.

A trial design dogma that deserves further consideration in emergent settings with relatively rapid outcome milestones relates to sample size. For drug development purposes the danger of small sample size studies providing seemingly significant results that are not reproducible and its counterpart of missing real treatment effects because a small study is less likely to separate a small signal from the background variability led to a professional attitude discouraging resisting small sample size pilots during the pandemic, but the policy tied up the available patient pool in smaller numbers of studies. The model of conducting community prospective studies of parallel treatment design if run in duplicate could potentially detect marginal signals from pooled data and also rapidly identify potent treatment effects as well as clearly ineffective or disease aggravating interventions that might otherwise not be appreciated.

In contending with a pandemic with significant mortality the objective of the research effort should be biased toward the more clinical substantial benefits. Policies to facilitate such prospective research in the primary care setting that otherwise are not staffed, equipped or structured to conduct traditional clinical research do research would be a prudent national policy.

I recommend readers review the pages of this tab starting with the original post.