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Evaluation of Clinical Trial Transparency in COVID-19 Vaccine Development (Pfizer/BioNTech, Moderna, AstraZeneca/Oxford).

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Abstract.

On or around August 10, 2020, Joyner, M.J. et al. [1] published results of a clinical study entitled "Effect of Convalescent Plasma on Mortality among Hospitalized Patients with COVID-19: Initial Three- Month Experience" in medRxiv (DOI: 10.1101/2020.08.12.20169359) which was sponsored by several United States Agencies. The Trump administration immediately seized upon the opportunity to publicize and claim credit for the sponsoring a clinical study that apparently supported Convalescent Plasma as a tremendous cure for COVID-19. The Commissioner of the United States Federal Drug Administration, Stephen Hann stated in a press conference that treatment of COVID-19 patients with Convalescent Plasma prevented death by 35%. However, upon examination of the of the paper by Joyner et al. [1], many Scientific Researchers have refuted the pronouncement of Stephen Hahn and pointed out that either Stephen Hahn does not understand rudimentary scientific statistics or he has committed the Dishonest Scientific Reporting and Data Falsification. The Clinical Trial of Joyner et al. [1] suffers from being frivolous as it has been designed to serve no scientific purpose, and it may have caused unnecessary deaths of participants. Joyner et al. [1] may have committed Scientific Misconduct through a violation of Scientific Ethics.

On or around August 10, 2020, Joyner, M.J. et al. [1] published results of a clinical study entitled "Effect of Convalescent Plasma on Mortality among Hospitalized Patients with COVID-19: Initial Three- Month Experience" in medRxiv (DOI: 10.1101/2020.08.12.20169359) which was sponsored by several United States Agencies, including, the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, National Center for Advancing Translational Sciences, National

Heart, Lung, and Blood Institute, National Institute of Diabetes and Digestive and Kidney Diseases Natural Sciences and Engineering Research Council of Canada, National Institute of Allergy and Infectious Disease, National Heart Lung and Blood Institute and National Institute on Aging. Desperate for any useful research item that would show that the Trump's administration was doing useful research to find a magic bullet for curing COVID-19, the Commissioner of the Federal Drug Administration, Stephen Hahn was given the task of selling Convalescent Plasma as a potential cure for COVID-19. On or around 2020, in a press conference, Stephen Hahn stated the following: (i) "So let me just put this in perspective. Many of you know I was a cancer doctor before I became FDA commissioner, and a 35% improvement in survival is a pretty substantial clinical benefit," Hahn continued. "What that means is — and if the data continue to pan out — 100 people who are sick with COVID-19, 35 would have been saved because of the administration of plasma", (ii) "In the optimal treatment — the optimal patients … treated with convalescent plasma at the highest titers . . . there was a 35% improvement in survival, which is a significant clinical benefit", and (iii) "So I would say that a 35 — if you're one of those 35 out of 100 people who these data suggest or show survive as a result of it . . . this is pretty significant for that person and their family". The Assistant Commissioner for Media Affairs, U.S. Food and Drug Administration tweeted the following: "Convalescent plasma has shown to be beneficial for 35%. This risk reduction figure - shown in chart below - is from @MayoClinic . . . ".

It is not clear where the 35% improvement in survival came from. What is clear is that the Commissioner of the Federal Drug Administration, Stephen Hahn had lied to American people and to the whole world. Nowhere in the paper by Joyner et al. [1] can one find a 35% improvement in survival. The study of Joyner cannot even determine whether Convalescent Plasma is effective at treating COVID-19 patients as there were no proper control in the open-label and uncontrolled study. Stephen Hahn had selectively used a snippet of data from Table 2 of the paper by Joyner et al [1] to come up with the misleading contention that Convalescent Plasma reduced mortality rate by 35%. The data in question concerned only 1076 COVID-19 patients out of a total of 35,322 COVID-19

patients who were treated with Convalescent Plasma. Joyner et al. [1] reported that the seven-day mortality rates for COVID-19 patients who were transfused with low IgG and high IgG were 13.7% (77 out of 561) and 8.9% (46 out of 515) respectively. Stephen Hahn calculated the difference between 13.7% and 8.9% (=4.8%) and using 13.7% as 100% death, Stephen Hahn came to the value of 35% improvement in survival. Stephen Hahn failed to inform the public that there was no proper control so that it was impossible to speak of improvement in survival and that it was also impossible to even speak of the effectiveness of Convalescent Plasma for the treatment of COVID-19 patients (See Figure 1 below which shows that Convalescent Plasma caused unnecessary death of COVID-19 patients). Stephen Hahn has committed Scientific Misconduct through Data Falsification and Dishonest Scientific Reporting. There is Data Falsification when scientific data is used selectively or manipulated to portray facts and conclusions that do not reflect the available scientific data [2,3]. There is Dishonest Scientific Report when scientific data or facts are ignored, discounted and not revealed so that proper scientific inferences cannot be made [2,3].

The Commissioner of the Federal Drug Administration, Stephen Hahn is not the sole guilty party. The study of Joyner et al. [1] must also be criticized because it was (i) unscientific. (ii) it was badly designed as it could not answer the important question of whether Convalescent Plasma could be effective at treating COVID-19 patients and whether Convalescent Plasma can prevent death of COVID-19 patients, (iii) it was performed in the absence of any consideration for the participants, and (iv) it caused unnecessary deaths.

In their study, Joyner et al. [1] have reported the following: (i) overall seven-day mortality rate of hospitalized COVID-19 patients who were transfused with Convalescent Plasma was 10.5% (ii) seven-day mortality rates for COVID-19 patients transfused with Convalescent Plasma for 18-39 age-group, 40-49 age-group, 50-69 age-group, 70-79 age-group and 80 and older age-group were 3.1% (109 out of 3472), 5.4% (662 out of 12168), 10.0% (897 out of 8968), 15.3% (1023 out of 6704), and 25.0% (1015 out of 4010), (iii) mortality rate for patients on ventilation prior to infusion was 17.6% (1685 out of 9573),

(iv) mortality rate for patients who were not on ventilation was 7.7 (1932 out of 25,205), (v) mortality rates for patients were administered with Convalescent Plasma 3 days or less, and 4 days or more than after hospitalization or diagnosis were 8.7% (1,340 out of 15407) and 11.9% (2,366 out of 19,915) respectively, and (vi) mortality rate for patients who were administered with Convalescent Plasma with low IgG, medium IgG and high IgG concentrations were 13.7% (77 out of 561), 11.6% (233 out of 2006) and 8.9% (46 out of 515) respectively.

In their study, Joyner et al. [1] have also reported the following: (i) overall thirty-day mortality rate of hospitalized COVID-19 patients who were transfused with Convalescent Plasma was 24.5% (ii) thirty-day mortality rates for COVID-19 patients transfused with Convalescent Plasma for 18-39 age-group, 40-49 age-group, 50-69 age-group, 70-79 age-group and 80 and older age-group were 7.5% (261 out of 3472), 15.1% (1,837 out of 12168), 27.1% (2431 out of 8968), 35.3% (2367 out of 6704), and 43.8% (1756 out of 4010), (iii) mortality rate for patients on ventilation prior to infusion was 41.0% (3924 out of 9573), (iv) mortality rate for patients who were not on ventilation was 17.9 (4523 out of 25,205), (v) mortality rates for patients were administered with Convalescent Plasma 3 days or less, and 4 days or more than after hospitalization or diagnosis were 21.6% (3229 out of 15407) and 26.7% (5,323 out of 19,915) respectively, and (vi) mortality rate for patients who were administered with Convalescent Plasma with low IgG, medium IgG and high IgG concentrations were 29.6% (166 out of 561), 27.4% (549 out of 2006) and 22.3% (115 out of 515) respectively.

Based on the above, one can argue that treatment of COVID-19 patients with Convalescent Plasma was not only harmful but also caused unnecessary deaths because of the following: The Average Mortality Rate of Hospitalized COVID-19 patients has been estimated to be ~3.7% in September 2020 from a high of 24.9% in March 2020 [4,5]. The overall Average Mortality Rate of Hospitalized COVID-19 patients can be estimated to be ~10.4%. It can therefore be deduced that Convalescent Plasma was harmful and caused unnecessary deaths of Hospitalized COVID-19 patients (Figure 1).

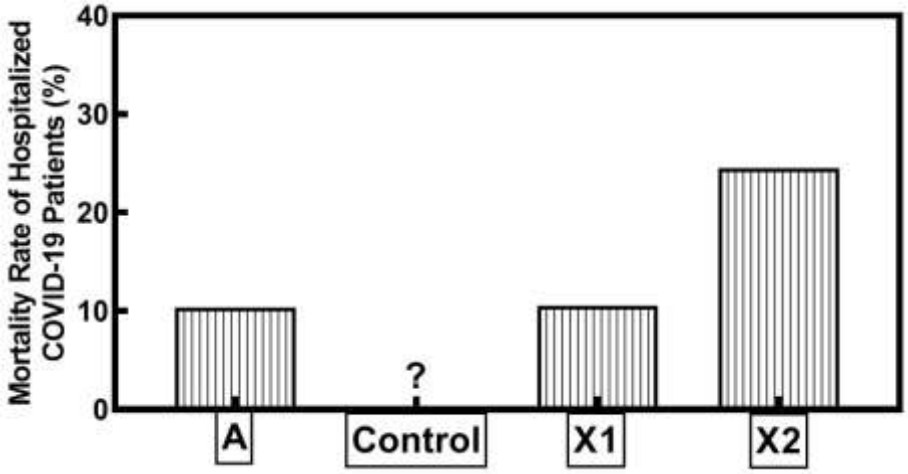

Figure 1. Mortality Rate of Hospitalized COVID-19 Patients (%). A: Average Mortality Rate of Hospitalized COVID-19 patients in the studies described in [4,5]. Control: There was no control in the study by Joyner et al. [1] X1: Overall Seven-Day Mortality Rate from the study of Joyner et al. [1]. X2: Overall Thirty-Day Mortality Rate from the study of Joyner et al. [1].

The study by Joyner et al. [1] may have caused very serious harm and unnecessary deaths if the Mortality Rates of Hospitalized COVID-19 patients who were not treated with Convalescent Plasma but who received Standard Treatment for the months of June 2020, July 2020, August 2020 and September 2020 are taken into consideration.

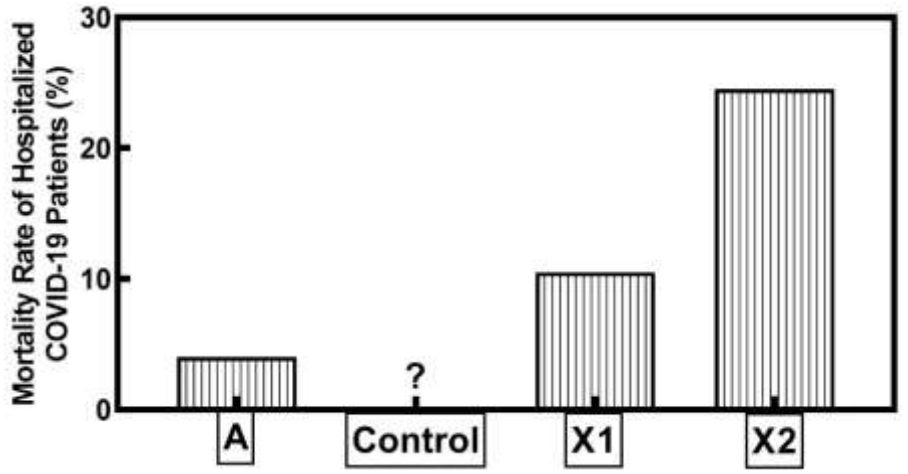

Figure 2. Mortality Rate of Hospitalized COVID-19 Patients (%). A: Average Mortality Rate of Hospitalized COVID-19 patients for the months of June 2020, July 2020, August 2020 and September 2020 in the studies described in [4,5]. Control: There was no control in the study by Joyner et al. [1] X1: Overall Seven-Day Mortality Rate from the study of Joyner et al. [1]. X2: Overall Thirty-Day Mortality Rate from the study of Joyner et al. [1].

Despite cautioning that "We did not indicate our study would prove efficacy or even offer potential help", Joyner et al. [1] concluded that "The relationships between mortality and both time to plasma transfusion, and antibody levels provide a signature that is consistent with efficacy for the use of convalescent plasma in the treatment of hospitalized COVID-19 patients". It can be said that Joyner et al. [1] have committed Scientific Misconduct via Dishonest Scientific Reporting and violation of Scientific Ethics.

References.

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