**Pandemic of Placebos in Covid-19**

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**Preamble**:

Within months of its emergence, Covid-19 has emerged as one of the world’s largest pandemics. High transmissibility of the virus and rapid spread from China to Europe, the Americas, South Asia and Africa, and devastation of economies in many countries has led to worldwide panic. Since public health response was initially slow and containment, prevention and treatment strategies not developed a veritable pandemic of misinformation and placebos has occurred. This pandemic has been fuelled by mainstream and social media and encompasses dubious public health interventions, preventive, curative and palliative treatments and data dredging.

**Public health**:

Classic public health response torapidly spreading respiratory infections has been promotion of isolation and quarantine.1 In Covid-19, modern diagnostic innovations led to rapid identification of virus structure and development of gene-based testing. Large scale contact tracing-testing-isolation (TTI) strategy was deployed early in the course of the epidemic in some countries with rapid containment. In countries where this strategy was delayed because of logistics (Southern Europe, USA, Brazil, South America) or costs (South Asia), infection has increased. Lack of the manpower required for TTI-strategy prompted many countries to deploy strategies such as prolonged lockdowns leading to economic hardships. The most useful individual level intervention for prevention of spread of the virus has been universal masking, hygiene and distancing.2 Flouting of these interventions has been the norm due to poor political and bureaucratic communication and has led to improper masking and physical crowding along with use of placebos such as inefficient designer masks, ineffective hand-sanitizers and high-cost air-purifiers. Masking is extremely important and is currently more protective than any other available intervention. Herd immunity through natural spread of infection or vaccines has been promoted. It is worth recalling that despite availability of effective vaccines, eradication of smallpox took 200 years and polio 60 years. Process of natural herd immunity kills more than it saves.1

**Prevention placebos**:

Since early phase of the epidemic prevention placebos focusing on two major pharmaceutical classes has been promoted- herbals and repurposed pharmaceuticals. Herbals include a number of designer placebos that are supposedly immunity boosters, antivirals and infection suppressants. Use of repurposed pharmacological agents such as antivirals, antimalarials, antihelminths and antibiotics is a greater concern.3 Support for some of these placebos is from politicians, politician-scientists and biased clinicians. A few national agencies have recommended emergency use authorization or developed national guidelines recommending large scale use of hydroxychloroquine as preventive therapies in absence of randomized trials.4 Social-media generated hype in these placebos led to widespread use as prophylaxis and treatment. In India, prescription of hydroxychloroquine, ivermectin and many similar drugs is widespread. Small randomized trials have not reported any benefit in disease prophylaxis while properly designed large scale studies are yet not available.

**Pharmacotherapy**:

Urgency to find a magic bullet has led to inadequately designed and underpowered clinical trials.3 Results have been published without high-quality peer review. List of such drugs include antivirals, antimalarials, antihelminths, antibiotics, immunomodulators, monoclonal and polyclonal antibodies, convalescent plasma and others. More than 3500 clinical trials are registered and NIH website has listed all published outcome trials.4 BMJ and WHO have created living update articles.3,5 Many of these drugs and combinations have failed in treatment of previous coronavirus infections (SARS-1, MERS, etc). On the other hand, rampant use of these potentially toxic drugs and drug-cocktails has been promoted based on misguided expert opinions and social media frenzy. Remdesivir, an antiviral medication is widely used after a few randomized trials reported benefit in reducing hospitalization duration with no influence on mortality. It has also received approval from US FDA. Results of larger trials are awaited. Examples of two expensive technologies that are widely used despite low quality evidence are revealing. Randomized trials of tocilizumab, an interfleukin-6 inhibitor, have failed to show benefit in hospitalized covid-19 patients.3,4 Convalescent plasma therapy has been promoted and approved by governments as panacea resulting in widespread use and creation of state-sponsored donor plasma banks. No large trial evidence exists.4 An medium-sized Indian randomized controlled trial has reported no benefit.6 Social media based medical education has led to massive public demand and subsequent widespread use of these drugs without much evidence. This has led to increase in healthcare costs and false hopes among patients and families.

**Statistics**:

Daily update in number of patients and deaths from covid-19 has led to global numbers-game and in countries with underground betting industry, punters are having a field day. Death statistics are misleading and often underreported. Number of excess deaths attributable to Covid-19 is more valid. Unfortunately in most developing countries such data are not available due to lack of robust vital registration system. Another placebo statistic is recovery rate*.* This is widely used to denote success and media gleefully highlights recoveries in 60-80%. Such numbers, in a disease with mortality rate of 2-5% and recovery in excess of 90%, instead of generating optimism is a serious indictment of health system. This rate does not account for almost a quarter of patients who have long-term sequelae. Daily update of this statistic has political dimensions and has been used for interstate dénouement in large countries such as India, USA and Brazil. Arm-chair statisticians, mathematicians and economists have led in production of national and international models to predict outcomes of the pandemic. All Covid-19 predictions have fallen by the wayside.

**Conclusions**:

Covid-19 pandemic has led to more than 850,000 deaths and has left millions with disability. It also has led to global panic and economic disaster. This has prompted use of placebos in public policies, preventive strategies, prophylactic drugs and untested therapies. Some of these placebos have led to unnecessary deaths and have greatly escalated costs of management of this largely self-limiting disease. Pandemics are controlled by public health practices and population education and not placebos.

**References**:

1. Ebrahim SH, Ahmed QA, Gozzer E, Schlagenhauf P, Memish ZA. Covid-19 and community mitigation strategies in a pandemic. BMJ. 2020; 368:m1066.
2. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks and eye protection to prevent person-to-person transmission in SARS-CoV-2 and Covid-19: a systematic review and meta-analysis. Lancet. 2020; 395;1973-1987.
3. Siemieniuk RA, Bartozsko JJ, Ge L, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. BMJ. 2020; 370:m2980.
4. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed 1 Sep 2020.
5. Lamontagne F, Agoritsas T, Macdonald H, et al. A living WHO guideline on drugs for Covid-19. BMJ. 2020; 370:m3379.
6. Agarwal A, Mukherjee A, Kumar G, et al. Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentric randomized controlled trial (PLACID Trial). BMJ. 2020; 371:m3939.