Update: June 30 - July 27, 2020

UPDATE ON GLOBAL REGIONAL AND NATIONAL DEVELOPMENTS ON COVID-19

THE KNOWLEDGE SYNTHESIS TEAM
CDT-AFRICA, ADDIS ABABA UNIVERSITY
www.cdt-africa.org

Summary

- As of July 27, 13.00 GMT, worldwide, more than sixteen million (16,451,551) people are now infected with coronavirus. Six million of them were diagnosed within the last one-month. The pandemic caused 652,921 deaths.
- As of July 27th, 4:00 PM EAT, a total of 844,542 cases 17,682 deaths and 489,948 recoveries from COVID-19 were reported in Africa.
- Further report on the impact of SARS-CoV-2 on children and adolescents aged below 21 years that, associated COVID-19 with Multisystem inflammatory syndrome that led to serious and life-threatening illness in this age group.
- The risk of mother to child transmission appears low with the appropriate precautions. Mothers could practice skin-to-skin care and breastfeed in the delivery room with the appropriate controlling measures.
- Antibody tests have low sensitivity during the first week of onset of symptoms (all less than 30.1%), rising in the second week and reaching their highest values in the third week.
- The WHO's Solidarity clinical trial has discontinued the hydroxychloroquine and Lopinavir/ritonavir arms of the trial in the inpatient study. However, studies on outpatients and prophylaxis are not affected.
- Large number of vaccine trials are underway and at-risk production is also reported in some countries. Phase 3 vaccine trial has also started.

Recommendations

- Consider including symptoms of loss of smell and taste in public education as important indicators of COVID-19 and for people with these experiences to take necessary precautions to protect themselves and others.
- Mothers could practice skin-to-skin care and breastfeed in the delivery room, but have to wear a mask when near their neonate and practice proper hand hygiene before skin-to-skin contact, breastfeeding, and routine care
- Antibody tests are useful but have important limitations that should be considered in interpretation of the studies: (1) have poor sensitivity in early stages of infection; (2) their sensitivity in milder illnesses is unclear because studies were done mostly in hospitalised patients; (3) their sensitivity after 6 weeks is not clear.
- Remdesivir may be useful for children and pregnant women (used on compassionate grounds). But this was based on report by the manufacturer, Gilead.

- Promising vaccine studies are being reported. Safety data need to be carefully considered.
- Combination of physical distancing measures (mass gatherings added to lock down and school closure) rather than single measures have been proven effective in controlling disease. Restrictions on transportation has not been shown to add effectiveness but context of implementation has to be considered.
- Guidelines on home-made cloth masks should stipulate multiple layers, at least 3.
    - Cloth masks should be washed daily and after high-exposure use by using soap and water or other appropriate methods
    - Face mask/coverings should be universal to have optimum effect
    - Face mask/coverings should be combined with social distancing.

Update on pathogenesis

Multisystem inflammatory syndrome in children

- A study was conducted with the aim of assessing the association between COVID -19 and Multisystem inflammatory syndrome among children below 21 years of age. The researchers conducted retrospective and prospective surveillance for Multisystem inflammatory syndrome from March 15 to May 20, 2020, in pediatric health centers across the United States. The major findings of the study are summarized as follow;
    - A total of 186 patients with inflammatory syndrome were identified in 26 states and 131(70%) were positive for SARS-CoV-2.
    - 148 (80%) patients were admitted in the intensive care unit, 37 (20%) received mechanical ventilation, 90 (48%) received vasoactive support, and 4 (2%) children died.
    - Majority [n=171 (92%)] of the patients had elevations in at least four bio-markers indicating inflammation.
    - Most patients [n=132 (71%)] had involvement of at least four organ systems; gastrointestinal [171 (92%)], cardiovascular [149 (80%)], hematologic [142 (76%)], mucocutaneous [137 [74%)], and respiratory [131 (70%)] systems.
    - Coronary-artery aneurysms and Kawasaki's disease like features were documented in 15 (8%) and 74 (40%) patients respectively.
- The study concluded that SARS-CoV-2 is associated with Multisystem inflammatory syndrome that led to serious and life-threatening illness in children and adolescents [Feldstein, L. R., 2020].

Mother to child transmission

- Previous studies indicated that vertical transmission of COVID-19 is unlikely; however, few neonates were found to be positive for SARS-CoV-2 and source of infection remained ambiguous. Recently, an observational study was done among 116 mothers who tested positive for SARS-CoV-2 and 120 neonates born between March 22 and May 17, 2020, at three Hospitals in New York City. Out of the total 120 neonates, 72 (60%) of them completed the follow-up and PCR tests was done at 24 hours, 5-7 days and 14 days of life.
- All (120) neonates were tested at 24 h of life and none were positive for SARS-CoV-2.
- A total of 82 and 72 neonates had a repeat PCR at 5–7 days and 14 days respectively; the result was negative in all and none of the neonates had symptoms of COVID-19.
- Of the 82 neonates at 5–7 days of life, 68 (83%) roomed in with the mothers and all mothers were allowed to breastfeed and 64 (78%) were breastfeeding until end of the follow up.
- The study suggested that mothers could practice skin-to-skin care and breastfeed in the delivery room, but have to wear a surgical mask when near their neonate and practice proper hand hygiene before skin-to-skin contact, breastfeeding, and routine care [Salvatore, C. M, et al, 2020].

Symptoms

- Loss of smell and taste was found to be discriminatory for people testing positive for COVID-19. This was based on self-reported symptoms of over 2.6 million participants from the UK and the US, with 18,401 having had SARS-CoV-2 test.
- This work, published in Nature Medicine, also identified a combination of symptoms, including anosmia, fatigue, persistent cough and loss of appetite, that together might identify individuals with COVID-19.

Update on Epidemiology (Incidence, mortality, recovery & epidemiologic parameters)

Global

- Worldwide, more than sixteen million (16,451,551) people are infected with coronavirus where six million of them were diagnosed within the last one month. The pandemic caused 652,921 deaths and 10,073,084 recoveries as of July 27, 13:00 GMT.
- Out of the total active cases, 5,659,142 (99%) had mild illness and only 66,404 (1%) are in critical or serious condition.

- The percentage of recoveries is gradually increasing and reached to 10,073,084 (94 %) while it was only 85 % at the beginning of the pandemic.
- On July 24th, additional 288,997 cases were reported globally which is the highest number of new cases recorded since the pandemic started, which reduced slightly in subsequent days [257,805 on July 25th and 221,743 on July 26th].
- United States of America (USA) continues to be the leading country with both high number of cases and deaths in the world. As of July 27th, 13:00 GMT, more than 4.3 million (4,372,056) people were infected with the virus and 149,852 deaths were reported in the country which accounted for 26.6 % of total cases and 22.9% of total deaths in the world.
- Other countries with high number of infections include Brazil (2,419,901), India (1,440,371), Russia (818,120), and South Africa (445,433).
- Brazil is also the second country with high number of deaths (87,052 deaths) followed by United Kingdom (45,752 deaths), Mexico (43,680) and Italy (35,107 deaths). However, South Africa (6,769) and Russia reported relatively lower number of deaths compared to the high morbidity rate in those countries.

Africa

- As of July 27th, 4:00 PM EAT, a total of 844,542 cases 17,682 deaths and 489,948 recoveries from COVID-19 were reported in Africa.
- The infection rate has increased substantially in South Africa, which currently accounts for over half of the cases in the continent (n=445,433; 52.7%). With this number, the country also ranked fifth worldwide.
- Egypt is the second most affected country with overall 92,062 cases contributing for 10.9% of total cases in Africa.
- Other African countries with high number of COVID-19 cases and deaths include; Nigeria (40,532 cases and 858 deaths), Ghana (32,969 cases and 168 deaths), Algeria (27,357 cases and 1,155 deaths) and Morocco (20,278 cases and 313 deaths).

Ethiopia

- Like other African countries, the number of corona cases was rapidly increasing in Ethiopia within the last one-month duration.
- A total of 131,735 laboratory tests were performed between June 30th to July 26th and additional 8,122 cases were identified in different regions of the country.
- The total number of deaths also increased from 103 to 223 and according to the ministry of health report, additional 3,786 people are fully recovered from the disease within the stated time frame.

- Therefore, a total of 382,339 laboratory tests were conducted and 13,968 confirmed cases, 223 deaths and 6,216 recoveries were reported as of July 26th, 2020.
- Out of the total 7,527 active cases, 65 of them are in critical condition and receiving treatment in the intensive care unit, while the others are having mild form of the disease.

Update on Diagnosis

- A systematic review of studies done on antibody tests, which included 54 publications and 25 data from 25 commercial tests and numerous in-house assays, was conducted. The pooled results for IgG, IgM, IgA, total antibodies and IgG/IgM all showed low sensitivity during the first week since onset of symptoms (all less than 30.1%), rising in the second week and reaching their highest values in the third week. It was noted these tests cannot have a primary role for the diagnosis of COVID-19 in the first week after symptom onset but they may still have a role complementing other testing in individuals presenting later, when RT-PCR tests are negative, or are not done. The combination of IgG/IgM had a sensitivity of 30.1% for 1 to 7 days, 72.2% for 8 to 14 days, 91.4% for 15 to 21 days. For 21 to 35 days, pooled sensitivities for IgG/IgM were 96.0%. It was stated antibody tests are likely to have a useful role for detecting previous SARS-CoV-2 infection if used 15 or more days after the onset of symptoms. It was noted the sensitivity has mainly been evaluated in hospitalised patients, so it is unclear whether the tests are able to detect lower antibody levels likely seen with milder and asymptomatic COVID-19 disease. It was indicated that there are insufficient studies to estimate sensitivity of tests beyond 35 days post-symptom onset which led the authors to conclude they are uncertain about the utility of these tests for sero-prevalence surveys for public health management purposes (Deeks and Van den Bruel, 2020).

Update on treatment

Solidarity Trial

- WHO accepted the recommendation from the Solidarity Trial's International Steering Committee to discontinue the trial's hydroxychloroquine and lopinavir/ritonavir arms. The International Steering Committee formulated the recommendation in light of the evidence for hydroxychloroquine vs standard-of-care and for lopinavir/ritonavir vs standard-of-care from the Solidarity trial interim results, and from a review of the evidence from all trials

presented at the 1-2 July WHO Summit on COVID-19 research and innovation. These interim trial results show that hydroxychloroquine and lopinavir/ritonavir produce little or no reduction in the mortality of hospitalized COVID-19 patients when compared to standard of care. For each of the drugs, the interim results do not provide solid evidence of increased mortality. There were, however, some associated safety signals in the clinical laboratory findings of the add-on Discovery trial, a participant in the Solidarity trial. This decision applies only to the conduct of the Solidarity trial in hospitalized patients and does not affect the possible evaluation in other studies of hydroxychloroquine or lopinavir/ritonavir in non-hospitalized patients or as pre- or post-exposure prophylaxis for COVID-19. The interim Solidarity results are now being readied for peer-reviewed publication (WHO 2020).

Dexamethasone

- In this controlled, open-label trial comparing a range of possible treatments in patients who were hospitalized with COVID-19, patients were randomly assigned to receive oral or intravenous dexamethasone (at a dose of 6 mg once daily) for up to 10 days or to receive usual care alone. The primary outcome was 28-day mortality. A total of 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. Overall, 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization (age-adjusted rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; P<0.001). The proportional and absolute between-group differences in mortality varied considerably according to the level of respiratory support that the patients were receiving at the time of randomization. In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94) but not among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55). Additionally, patients in the dexamethasone group had a shorter duration of hospitalization than those in the usual care group (median, 12 days vs. 13 days) and a greater probability of discharge alive within 28 days (rate ratio, 1.10; 95% CI, 1.03 to 1.17). The greatest effect regarding discharge within 28 days was seen among patients who were receiving invasive mechanical ventilation at randomization. Among the patients who were not receiving invasive mechanical ventilation at randomization, the number of patients who

progressed to the prespecified composite secondary outcome of invasive mechanical ventilation or death was lower in the dexamethasone group than in the usual care group (risk ratio, 0.92; 95% CI, 0.84 to 1.01). This effect was greater among the patients who were receiving oxygen at randomization. In conclusion, in patients hospitalized with Covid-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support (Group et al. 2020).

Remdesivir

- According to a virtual scientific conference on July 10, Gilead Sciences Inc reported that Remdesivir can not only speed recovery, but may cut the chance of dying of COVID-19. Among severely sick people, the antiviral drug reduced the risk of dying by 62 percent compared with standard care. Hospitalized people taking remdesivir had a 7.4 percent death rate two weeks after treatment started, while those not taking the drug had a 12.5 percent mortality rate, the company reported. The new data come from two studies: a Phase III study of 312 patients, which was aimed at studying the efficacy of the drug, and a study that retrospectively examined the effect of the drug in 818 people with COVID-19. The company also found that 74.4 percent of people taking remdesivir recovered by day 14, compared with 59 percent of those getting standard care (ScienceNews 2020).
- Gilead also reported data on remdesivir given for "compassionate use" to children and pregnant women: Of 77 pediatric patients taking remdesivir, 73 percent, or 56 kids, were released from the hospital by day 28. Twelve percent remained hospitalized but breathing on their own without needing extra oxygen, and 4 percent died. Among 86 infected women, the drug helped lessen the amount of extra oxygen needed in 96 percent of pregnant women and 89 percent of women who had newly given birth. It is important to cautiously interpret these results the full report of these studies is published (ScienceNews 2020).

Update on Vaccine

mRNA - 1273

- A Preliminary report on phase 1 open-label trial of the mRNA -1273 vaccine was published on the New England Journal of Medicine. The trial was conducted at the Kaiser Permanente Washington Health Research Institute in Seattle and at the Emory University School of

Medicine in Atlanta. The trial included 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25 μg, 100 μg, or 250 μg. There were 15 participants in each dose group. No serious adverse events were noted, and no prespecified trial halting rules were met. One participant in the 25-μg group was withdrawn because of an unsolicited adverse event, transient urticaria, judged to be related to the first vaccination. After the first vaccination, solicited systemic adverse events were reported by 5 participants (33%) in the 25-μg group, 10 (67%) in the 100-μg group, and 8 (53%) in the 250-μg group; all were mild or moderate in severity. The two-dose vaccine series was generally without serious toxicity; systemic adverse events after the first vaccination, when reported, were all graded mild or moderate. Greater reactogenicity followed the second vaccination, particularly in the 250-μg group. Across the three dose groups, local injection-site reactions were primarily mild (Jackson, Anderson et al. 2020).

- The mRNA-1273 vaccine was immunogenic, inducing robust binding antibody responses to both full-length S-2P and receptor-binding domain in all participants after the first vaccination in a time- and dose-dependent fashion. Commensurately high neutralizing antibody responses were also elicited in a dose-dependent fashion. Seroconversion was rapid for binding antibodies, occurring within 2 weeks after the first vaccination, but pseudo virus neutralizing activity was low before the second vaccination, which supports the need for a two-dose vaccination schedule. It is important to note that both binding and neutralizing antibody titers induced by the two-dose schedule were similar to those found in convalescent serum specimens. However, interpretation of the significance of those comparisons must account for the variability in Covid-19 convalescent antibody titers according to factors such as patient age, disease severity, and time since disease onset and for the number of samples in the panel(Jackson, Anderson et al. 2020).
- These safety and immunogenicity findings support advancement of the mRNA-1273 vaccine to later-stage clinical trials. Of the three doses evaluated, the 100-μg dose elicits high neutralization responses and Th1-skewed CD4 T cell responses, coupled with a reactogenicity profile that is more favorable than that of the higher dose. A phase 2 trial of mRNA-1273 in 600 healthy adults, evaluating doses of 50 μg and100 μg, is ongoing (Jackson et al. 2020). According to the NIH, a Phase 3 clinical trial has just begun. The study is expected to enroll approximately30,000 adult volunteers who do not have COVID-19 (https://www.nih.gov/news-events/news-releases/phase-3-clinical-trial-investigational-vaccine-covid-19-begins)

ChAdOx1 nCoV-19(AZD1222) study.

- The study was a phase 1/2 single-blind, randomised controlled trial of ChAdOx1 nCoV-19 compared with a licensed meningococcal group A, C, W-135, and Y conjugate vaccine (MenACWY; Nimenrix, Pfizer, UK), as control vaccine, in healthy adults in the UK. The trial investigated the immunogenicity, reactogenicity, and safety of vaccination with 5×10^{10} viral particles of ChAdOx1 nCoV-19 in single-dose and two-dose regimens. 1077 participants were enrolled into the study and assigned to vaccination with either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomized ChAdOx1 nCoV-19 group. The preliminary findings show that the candidate ChAdOx1 nCoV-19 vaccine given as a single dose was safe and tolerated, despite a higher reactogenicity profile than the control vaccine, MenACWY. No serious adverse reactions to ChAdOx1 nCoV-19 occurred. The majority of adverse events reported were mild or moderate in severity, and all were self-limiting (Folegatti et al. 2020). However, local and systemic reactions were reduced by use of prophylactic paracetamol.
- Humoral responses to SARS-CoV-2 spike protein peaked by day 28 post prime and cellular responses were induced in all participants by day 14. Neutralising antibodies were induced in all participants after a second vaccine dose. After two doses, potent cellular and humoral immunogenicity was present in all participants studied (Folegatti et al. 2020).

Adenovirus type-5-vectored COVID-19 vaccine

- This randomised, double-blind, placebo-controlled, phase 2 trial of the Ad5-vectored COVID-19 vaccine was done in a single centre in Wuhan, China. Healthy adults aged 18 years or older, who were HIV-negative and previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection-free, were eligible to participate and were randomly assigned to receive the vaccine at a dose of 1×10^{11} viral particles per mL or 5×10^{10} viral particles per mL, or placebo. The primary endpoints for immunogenicity were the geometric mean titres (GMTs) of specific ELISA antibody responses to the receptor binding domain (RBD) and neutralising antibody responses at day 28. The primary endpoint for safety evaluation was the incidence of adverse reactions within 14 days. All recruited participants who received at least one dose were included in the primary and safety analyses. 508 eligible participants (50% male; mean age 39·7 years, SD 12·5) consented to participate in the trial and were randomly assigned to receive the vaccine (1×10^{11} viral particles n=253; 5×10^{10} viral particles n=129) or placebo (n=126). In the 1×10^{11} and 5

× 10^{10} viral particles dose groups, the RBD-specific ELISA antibodies peaked at 656·5 (95% CI 575·2–749·2) and 571·0 (467·6–697·3), with seroconversion rates at 96% (95% CI 93–98) and 97% (92–99), respectively, at day 28. Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2, with GMTs of 19·5 (95% CI 16·8–22·7) and 18·3 (14·4–23·3) in participants receiving 1 × 10^{11} and 5 × 10^{10} viral particles, respectively. Specific interferon γ enzyme-linked immunospot assay responses post vaccination was observed in 227 (90%, 95% CI 85–93) of 253 and 113 (88%, 81–92) of 129 participants in the 1 × 10^{11} and 5 × 10^{10} viral particles dose groups, respectively. Solicited adverse reactions were reported by 183 (72%) of 253 and 96 (74%) of 129 participants in the 1 × 10^{11} and 5 × 10^{10} viral particles dose groups, respectively. Severe adverse reactions were reported by 24 (9%) participants in the 1 × 10^{11} viral particles dose group and one (1%) participant in the 5 × 10^{10} viral particles dose group (Zhu, Guan et al. 2020).

- The study removed the age cap for the recruitment of participants for this phase 2 trial. Older individuals (i.e., aged ≥55 years), many of whom often have chronic illness, have a high risk of serious illness and death associated with SARS-CoV-2 infection; thus, they are an important target population for a COVID-19 vaccine. The results suggest a single-dose immunisation schedule of Ad5-vectored COVID-19 vaccine at 5 × 10^{10} viral particles is an appropriate regimen for healthy adults. Compared with the younger population, results indicated older people to have a significantly lower immune response, but higher tolerability, to the Ad5-vectored COVID-19 vaccine. Therefore, an additional dose might be needed to induce a better immune response in the older population, and this will be evaluated in a phase 2b trial (Zhu et al. 2020).
- The study concluded that the candidate Ad5-vectored COVID-19 vaccine has a good safety profile, with only mild, transient adverse events related to vaccination and no serious adverse events. Single-dose immunisation with the vaccine induced rapid onset of immune responses within 14 days and significant humoral and cellular immune responses within 28 days in the majority of the recipients. The researchers are planning an international multicentre, randomised, double blind, controlled phase 3 effectiveness trial to further evaluate the efficacy of the vaccine (Zhu, Guan et al. 2020).

BNT162b1

- BioNTech SE and Pfizer Inc announced initial data from their ongoing German Phase 1/2, open-label, non-randomized, non-placebo-controlled, dose-escalation trial, that is part of the global mRNA-based vaccine program against SARS-CoV-2. Preliminary data for

BNT162b1 in the German Phase 1/2 trial were evaluated with a total of 60 healthy adults 18 to 55 years of age enrolled in the study. Of these 60 participants, 12 subjects per dose level (1 µg, 10 µg, 30 µg, and 50 µg; 48 participants in total), were vaccinated with BNT162b1 on day 1 and day 22 (n=12 per prime-boost cohort, except n=11 for the 10 µg and 50 µg cohorts from day 22 on). Furthermore, 12 participants received a single injection of 60 µg(PFIZER. 2020).

- The vaccine elicited high, dose level-dependent SARS-CoV-2-neutralizing titers and RBD-binding IgG concentrations after the second dose. Day 43 SARS-CoV-2 neutralizing geometric mean titers were in the range of 0.7-fold (1 µg) to 3.2-fold (50 µg) compared to that of a panel of SARS-CoV-2 infection convalescent human sera. Furthermore, sera of vaccinated subjects displayed broadly neutralizing activity in pseudovirus neutralization assays across a panel of sixteen SARS-CoV-2 RBD variants represented in publicly available SARS-CoV-2 sequences and against the newly dominant D614G strain(PFIZER. 2020).
- In addition, the initial German trial results demonstrate, for the first time for the BNT62b1 candidate, a concurrent induction of high level CD4+ and CD8+ T cell responses against the SARS-CoV-2 RBD. the strength of T cell responses varied between subjects. There was no clear dose level dependency of the T cell response between 1 µg to 50 µg, indicating that stimulation and robust expansion of T cells might be accomplished at low mRNA dose levels(PFIZER. 2020).
- Overall, the data suggested that BNT162b1 could potentially be administered safely, with a manageable tolerability profile. Local reactions and systemic events after injection with BNT162b1 at all dose levels were transient, generally mild to moderate, with occasional severe events (Grade 3) of flu-like symptoms and injection site reactions. All adverse events resolved spontaneously and were managed with simple measures. No serious adverse events (SAEs) were reported, and there were no withdrawals due to adverse events related to the vaccine(PFIZER. 2020).

INO 4800

- INOVIO Announces Positive Interim Phase 1 Data For INO-4800 Vaccine for COVID-19. The Phase 1 clinical trial of INO-4800 initially enrolled 40 healthy adult volunteers 18 to 50 years of age at two U.S. sites with funding from the Coalition for Epidemic Preparedness Innovations (CEPI). The participants were enrolled into 1.0 mg and 2.0 mg dose cohorts; each participant received two doses of INO-4800 four weeks apart. Each dose was administered by intradermal injection using INOVIO's CELLECTRA® 2000 device. An

independent Data Safety Monitoring Board reviewed the safety data. INO-4800 was generally safe and well-tolerated in all participants in both cohorts through week 8; all ten reported adverse events (AEs) were grade 1 in severity, and most were local injection site redness. There were no reported serious adverse events (SAEs). INOVIO to begin U.S. Phase 2/3 efficacy study this summer upon regulatory concurrence(INOVIO 2020).

Update on Public Health Control Measures

- Globally, countries continue to employ various interventions aiming to control the COVID-19 pandemic. Physical distancing (interchangeably referred to as social distancing) is among the commonest interventions. Majority of the studies so far that have investigated the effectiveness of interventions in controlling SARS-Cov-2 transmission were model based. But a recent study compared the incidence rate (IR) of COVID-19 before and after the implementation of physical distancing policies (i.e. school closure, workplace closure, restrictions on mass gathering, public transport closure, and lockdowns) in 149 countries globally.
- A pooled estimate from all the study countries indicated a 13% decrease in the incidence of COVID-19 attributable to the combined physical distancing measures. This reduction is unaffected by the time when the interventions were in effect (counting from when the first case was detected) and the number of people tested for COVID-19. However, percentage of the population older than 65 years, higher GDP per capita, and higher country security index were associated with a greater reduction in the Incidence Rate Ratio (IRR).
- The number of physical distancing interventions (out of the mentioned five) showed no significant difference in the IRR when implementing a combination of five or four interventions, regardless of the types of intervention. But a significant decrease in IRR was reported when a combination of three interventions were compared with five.
- The most effective combination of interventions to reduce incidence of the disease included mass gatherings added to lock down and school closure which were implemented early on. However, no additional benefit was obtained when restricting public transport was added to the remaining physical distancing measures. But this finding should be viewed in the context of the intervention countries.

Update on personal protective equipment

Face mask use

- New studies have been published cloth masks. (1) The efficacy of cloth masks is lower than medical masks and that its filtration ability depends on thread count, number of layers, type of fabric, and water resistance. (2) Cloth masks are more suitable option for community use when medical masks are unavailable. (3) Cloth masks should be washed daily and after high-exposure use by using soap and water or other appropriate methods (Chughtai et al., 2020).
- Additional study evaluated the effectiveness of the CDC recommended one- and two-layer cloth face covering against a three-ply surgical mask by challenging the cloth covering against speaking, coughing and sneezing. A tailored LED lighting system was used to provide visual evidence of the efficacy of face coverings. The captured video showed, for speaking, a single-layer cloth face covering reduced the droplet spread but a double-layer covering performed better. However, a double-layer cloth face covering was significantly better at reducing the droplet spread caused by coughing and sneezing. A surgical mask was the best among all the tested scenarios in preventing droplet spread from any respiratory emission. It was concluded that guidelines on home-made cloth masks should stipulate multiple layers, at least 3 (Bahl et al., 2020).
- A modelling study, which took the possibility of assortative mixing, where mask users interact preferentially with other mask users, into account made three key observations; [1] Masks, even with suboptimal efficacy in both prevention of acquisition and transmission of infection, could substantially decrease the reproduction number for COVID-19 if widely used, [2] Widespread masking may be sufficient to suppress epidemics where R has been brought close to 1 via other measures (e.g., distancing), [3] "Assortment" within populations (the tendency for interactions between masked individuals to be more likely than interactions between masked and unmasked individuals) would rapidly erode the impact of masks. The authors indicated mask uptake needs to be fairly universal to have an effect and that this simple model suggests that widespread uptake of masking could be determinative in suppressing COVID-19 epidemics in regions with R(t) at or near 1(Fisman et al., 2020)

Reference list

- African Union; COVID -19 updates. https://au.int/en/covid19
- BAHL, P., BHATTACHARJEE, S., DE SILVA, C., CHUGHTAI, A. A., DOOLAN, C. & MACINTYRE, C. R. 2020. Face coverings and mask to minimise droplet dispersion and aerosolisation: a video case study. Thorax, thoraxjnl-2020-215748.
- Center of Disease Control and Prevention Africa https://africacdc.org/covid-19-update/
- CHUGHTAI, A. A., SEALE, H. & MACINTYRE, C. R. 2020. Effectiveness of Cloth Masks for Protection Against Severe Acute Respiratory Syndrome Coronavirus 2. Emerg Infect Dis.
- DEEKS, J. J. D. J. T. Y. D. C. S. R. T.-P. S. A. A. B. S. D. J. F. D. R. L. H. I. & VAN DEN BRUEL, A. 2020. Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database of Systematic Reviews.
- Ethiopian Public Health Institute CoronaVirus Update; https://www.ephi.gov.et/index.php/public-health-emergency/novel-corona-virus-update
- Feldstein, L. R., Rose, E. B., Horwitz, S. M., Collins, J. P., Newhams, M. M., Son, M. B. F., Randolph, A. G. (2020). Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med, 383(4), 334-346. doi: 10.1056/NEJMoa2021680
- FISMAN, D. N., GREER, A. L. & TUITE, A. R. 2020. Bidirectional impact of imperfect mask use on reproduction number of COVID-19: A next generation matrix approach. Infect Dis Model, 5, 405-408.
- Folegatti, P. M., K. J. Ewer, P. K. Aley, B. Angus, S. Becker, S. Belij-Rammerstorfer, D. Bellamy, S. Bibi, M. Bittaye, E. A. Clutterbuck, C. Dold, S. N. Faust, A. Finn, A. L. Flaxman, B. Hallis, P. Heath, D. Jenkin, R. Lazarus, R. Makinson, A. M. Minassian, K. M. Pollock, M. Ramasamy, H. Robinson, M. Snape, R. Tarrant, M. Voysey, C. Green, A. D. Douglas, A. V. S. Hill, T. Lambe, S. C. Gilbert, A. J. Pollard and C. V. T. G. Oxford (2020). "Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial." Lancet.
- Group, R. C., P. Horby, W. S. Lim, J. R. Emberson, M. Mafham, J. L. Bell, L. Linsell, N. Staplin, C. Brightling, A. Ustianowski, E. Elmahi, B. Prudon, C. Green, T. Felton, D. Chadwick, K. Rege, C. Fegan, L. C. Chappell, S. N. Faust, T. Jaki, K. Jeffery, A. Montgomery, K. Rowan, E. Juszczak, J. K. Baillie, R. Haynes and M. J. Landray (2020). "Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report." N Engl J Med.

- HOLMES, E. A., O'CONNOR, R. C., PERRY, V. H., TRACEY, I., WESSELY, S., ARSENEAULT, L., BALLARD, C., CHRISTENSEN, H., SILVER, R. C. & EVERALL, I. 2020. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. The Lancet Psychiatry.
- INOVIO. (2020, 30 June 2020). "INOVIO Announces Positive Interim Phase 1 Data For INO-4800 Vaccine for COVID-19." Retrieved 24 July 2020, from http://ir.inovio.com/news-releases/news-releases-details/2020/INOVIO-Announces-Positive-Interim-Phase-1-Data-For-INO-4800-Vaccine-for-COVID-19/default.aspx.
- Islam N, Sharp SJ, Chowell G, Shabnam S, Kawachi I, Lacey B, et al. Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries. British Medical Journal 2020;370.
- Jackson, L. A., E. J. Anderson, N. G. Rouphael, P. C. Roberts, M. Makhene, R. N. Coler, M. P. McCullough, J. D. Chappell, M. R. Denison, L. J. Stevens, A. J. Pruijssers, A. McDermott, B. Flach, N. A. Doria-Rose, K. S. Corbett, K. M. Morabito, S. O'Dell, S. D. Schmidt, P. A. Swanson, M. Padilla, J. R. Mascola, K. M. Neuzil, H. Bennett, W. Sun, E. Peters, M. Makowski, J. Albert, K. Cross, W. Buchanan, R. Pikaart-Tautges, J. E. Ledgerwood, B. S. Graham and J. H. Beigel (2020). "An mRNA Vaccine against SARS-CoV-2 — Preliminary Report." New England Journal of Medicine.
- John Hopkins, Corona Virus Resources https://coronavirus.jhu.edu/map.html
- MCALONAN, G. M., MURPHY, D. G. & EDWARDS, A. D. 2020. Multidisciplinary: research priorities for the COVID-19 pandemic. The Lancet Psychiatry, 7, e35.
- MORGAN, C. & ROSE, N. 2020. Multidisciplinary research priorities for the COVID-19 pandemic. The lancet. Psychiatry, 7, e33.
- PFIZER. (2020, 20 July 2020). "PFIZER AND BIONTECH ANNOUNCE EARLY POSITIVE UPDATE FROM GERMAN PHASE 1/2 COVID-19 VACCINE STUDY, INCLUDING FIRST T CELL RESPONSE DATA." Retrieved 24 July 2020, from https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-early-positive-update-german.
- Salvatore, C. M., Han, J.-Y., Acker, K. P., Tiwari, P., Jin, J., Brandler, M., DeLaMora, P. (2020). Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study. The Lancet Child & Adolescent Health. doi: 10.1016/s2352-4642(20)30235-2
- ScienceNews. (2020, 13/07/2020). "Remdesivir may work even better against COVID-19 than we thought." Retrieved 24/07/2020, from

https://www.sciencenews.org/article/remdesivir-covid-19-coronavirus-pandemic-gilead.

- WHO. (2020, 04/07/2020). "WHO discontinues hydroxychloroquine and lopinavir/ritonavir treatment arms for COVID-19." Retrieved 24/07/2020, from https://www.who.int/news-room/detail/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-covid-19.
- World Health Organization: https://www.who.int/images/default-source/health-topics/coronavirus/pregnancy-breastfeeding/who---pregnancy---5.png
- Worldometer, Corona Virus https://www.worldometers.info/coronavirus/
- Zhu, F.-C., X.-H. Guan, Y.-H. Li, J.-Y. Huang, T. Jiang, L.-H. Hou, J.-X. Li, B.-F. Yang, L. Wang, W.-J. Wang, S.-P. Wu, Z. Wang, X.-H. Wu, J.-J. Xu, Z. Zhang, S.-Y. Jia, B.-S. Wang, Y. Hu, J.-J. Liu, J. Zhang, X.-A. Qian, Q. Li, H.-X. Pan, H.-D. Jiang, P. Deng, J.-B. Gou, X.-W. Wang, X.-H. Wang and W. Chen (2020). "Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial." The Lancet.