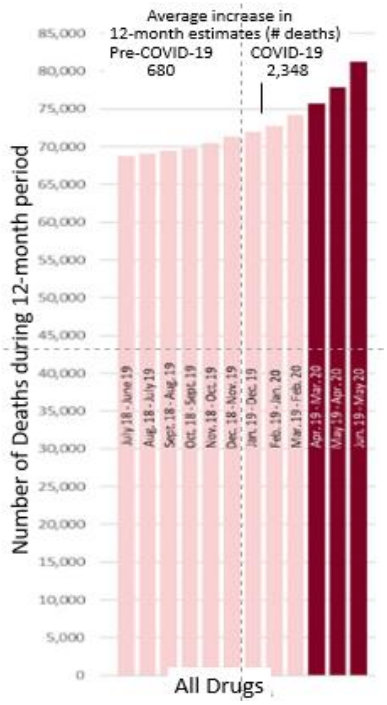
COVID-19 LITERATURE BRIEFING
December 23rd, 2020

Children's MINNESOTA

Reference of the Week

- Centers for Disease Control and Prevention. Distributed via the CDC Health Alert Network: 12.17.2020. HAN00438.



https://emergency.cdc.gov/han/2020/han00438.asp

Providers Alerted: public health departments, providers, first responders, harm reduction organizations, labs, medical examiners and coroners.

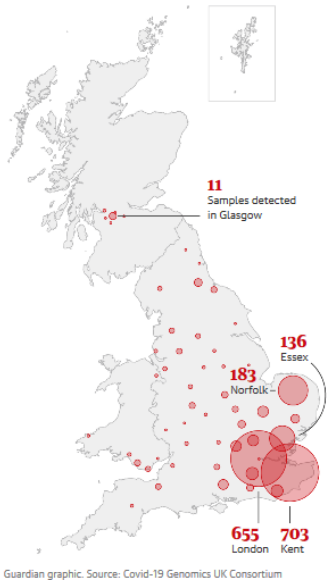
Concerns: 1. Substantial increases in drug overdose deaths, especially illicitly manufactured fentanyl. **2.** The largest increase in overdose deaths has taken place from March 2020 to May 2020 coinciding with COVID-19 mitigation measures. **3.** Increases in overdose deaths with psychostimulants such as methamphetamine has occurred as well.

Recommendations: 1. Expand the provision and use of naloxone and overdose prevention education. **2.** Expand access to and provision of treatment for substance use disorders. **3.** Intervene early with individuals at the highest risk for overdose particularly those leaving correctional and detention centers. **4.** Improve detection of overdose outbreaks due to fentanyl, novel psychoactive substances (e.g., fentanyl analogs), or other drugs to facilitate an effective response.

*Noteworthy is a > 20% increase in fatal drug overdose in **Minnesota** from 12-months ending in June 2019 to 12 months ending in May 2020 with the trend continuing through June 2020. Children and adolescents who grow up in households with opioid misuse and may experience a myriad of adverse consequences, including: increased risk of mental health problems and drug use; accidental opioid poisoning; increased risk of developing a substance use disorder; and family dissolution that results from parents' incarceration, foster care placement, or loss of parent to an opioid overdose.* (See,Winstanley EL. The impact of the opioid epidemic on children and adolescents. Clin Ther. 2019;41:1655-1662)

Other References:

- New COVID-19 variant concerns create confusion and stronger mitigation measures in England:



1. 12/19/20. Boris Johnson/science panel announces that a "new" strain of the virus that has been in circulation since November may be "up to 70% more transmissible . . . there is no evidence to suggest that it is more lethal . . . there is no evidence to suggest that vaccines will be any less effective." It is now the predominant strain in England.

2. 12/20/20. New tier 4 restrictions implemented in England and Ireland: stay at home; limit holiday gatherings; and closure of non-essential retail. 40 countries have banned travel and freight handled by human hands from England.

3. 12/21/20. WHO news conference reiterates the concern for the SARS-CoV-2 D117 lineage spreading in England. Experts emphasize the paucity of information on the variant suggesting that the purported increase in transmission may in part be due to human behavior. If the variant increases the transmission as suggested then the R_0 may increase by 0.4 to 0.9 to a level of 1.4 to 1.9 despite all the current and past efforts.

4. 12/22/20. The CDC assumes the new variant is circulating in the US though it has not yet been detected.

SEE THE ARTICLE CABINET ON THE S: DRIVE, "COVID-19 ARTICLE RESOURCE CABINET" FOR CHILDREN'S FULL COLLECTION

- Faust JS. All-Cause Excess Mortality and COVID-19–Related Mortality Among US Adults Aged 25-44 Years, March-July 2020. JAMA network. 12.16.2020. Research letter. https://jamanetwork.com/journals/jama/fullarticle/2774445 pdf
  Premise/Methods: 1. Information on mortality in young adulthood is lacking and too often COVID-19 is considered deadly only to the aged. **2.** Excess mortality reflects the full burden of the pandemic minimizing uncoded COVID-19 deaths and deaths not due to infection but may be pandemic related. **3.** Autoregressive moving averages (using prior observations to predict future values, in this case deaths) of mortality data from 2015-2019 were compared to 2020 age-stratified mortality data from the entire country.
  Results: 1. From March 1, 2020, to July 31, 2020, a total of 76 088 all-cause deaths occurred among US adults aged 25 to 44 years, which was 11 899 more than the expected 64 189 deaths. **2.** COVID-19 accounted for 38% of the excess deaths which may reflect under-detection as opioid related deaths were similar to data from 2018. **3.** COVID-19 and opioid fatalities are the two leading causes of deaths in adults 25-44 years of age and are numerically similar.

- Piroth L. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. The Lancet, respiratory medicine. 12.17.2020. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30527-0/fulltext pdf
  Premise/Methods: 1. COVID-19 and influenza are both respiratory diseases that differ in outcomes. **2.** To date, no large scale clinical comparisons between the two pathogens exist. **3.** This is a French retrospective clinical comparison of hospitalized patients with influenza from 12/1/18 through 2/28/19 and COVID-19 from 3/1/20 to 4/30/20. **4**. Comparisons of risk factors, clinical characteristics, and outcomes between patients hospitalized for COVID-19 and influenza were done, with administrative data also stratified by age group.
  Results: 1. The study captured 89 530 patients with COVID-19 and 45 819 patients with influenza: the median age for COVID-19 was 68 years and influenza 71 years; fewer pediatric patients had COVID-19 than influenza (1227 vs 8942); but a larger proportion of patients younger than 5 years needed intensive care support for COVID-19 than for influenza (2.3% vs 0.9%). **2.** Mortality in young children was too infrequent for both diseases to make a comparison. **3.** Patients with COVID-19 were more frequently obese or overweight, and more frequently had diabetes, hypertension, and dyslipidaemia than patients with influenza, whereas those with influenza more frequently had heart failure, chronic respiratory disease, cirrhosis, and deficiency anaemia. **4.** Hospitalized COVID-19 patients were more likely to experience respiratory failure, pulmonary embolism, stroke, septic shock, ICU stays were twice as long for COVID-19, and in-hospital mortality was three times as great for COVID-19.
  Buried in the data is a ten-fold increase in mortality with COVID-19 in the 11-17 year age group compared to influenza with obesity or being overweight a risk factor for death. No attempt was made to determine the incidence of MIS-C in this study.

- Weinreich DM. REGN-COV2, a neutralizaing antibody cocktail, in outpatients with Covid-19. NEJM. https://www.nejm.org/doi/full/10.1056/NEJMoa2035002 pdf
  Premise/Methods: 1. REGN-COV2 is a cocktail made up of two neutralizing human IgG1 antibodies that target the SARS-CoV-2 spike protein, thereby preventing viral entry into human cells through the ACE2 receptor. **2.** Each of the two antibodies that make up REGN-COV2 — casirivimab (REGN10933) and imdevimab (REGN10987) — is given in equal doses in the cocktail. **3.** This is an interim report of a multicenter, randomized, double blind, placebo-controlled trial involving symptomatic, non-hospitalized patients with COVID-19. **4.** In the phase 1–2 portion of the trial reported here, all patients were randomly assigned (1:1:1) to receive placebo, REGN-COV2 at a dose of 2.4 g (low dose), or REGN-COV2 at a dose of 8.0 g (high dose).
  Results: 1. 275 patients were enrolled: patients were 18 years and older; tested positive for SARS-CoV-2 within 72 hours of randomization and within 7 days of symptom onset; median age was 44 years, 13% of participants were African American and 56% Latinx; at baseline, 123 patients (45%) were serum antibody–positive, 113 (41%) were serum antibody–negative, and 39 (14%) had unknown antibody status; 90 received high dose and 92 low dose; **2.** Patients were designated as antibody positive or negative depending on the status of serum anti-SARS-CoV-2 antibody. **3.** REGN-COV2 enhanced clearance of virus, particularly in serum antibody–negative subjects or who had a high viral load at baseline. Furthermore, the neutralizing titers achieved with REGN-COV2 were more than 1000 times the titers achievable with convalescent-phase plasma, and REGN-COV2 had a profound and rapid effect on viral load, **4.** REGN-COV2 did not improve the reduction in viral load in antibody positive subjects suggesting that native immunity was effective and in part explains the mild nature of COVID-19 in most people.

REGN-COV2 received an EUA in November. Its potential advantage over other antibody products rests with a cocktail of two antibodies likely conferring some protection to viral mutation and resistance. Bamlanivimab, a Lilly monoclonal, has an EUA down to age 12 year.