

COVID-19 in Pregnancy

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Conflicts of Interest

- I review for Up To Date but not regarding this topic
- Off label use of medications will be discussed and clearly identified

MAN WITH CORONA VIRUS

Corona,
Extra

SEEKS WOMAN WITH LYME DISEASE

imgflip.com

Terminology

- Corona betaviruses: family of “cold” viruses spread by airborne droplets and close personal contact
- Novel corona virus SARS-CoV-2 (causes COVID-19 infection)
 - Corona variant
 - Originated in China
 - Jump from bats to animals to humans
- SARS-CoV
 - Originated in Hong Kong
 - Jump from bats to palm civets to humans
- MERS-CoV
 - Originated in Middle East
 - Jump from bats to camels to humans



SARS-CoV: Severe Acute Respiratory Syndrome

- Guangdong China
- Symptoms initial 5-7 days:
 - URI
 - Low grade fever (<100.4F; <38C)
 - Diarrhea
- Respiratory distress phase days 8-12
 - Median day requiring intubation 8
- Recovery phase days 14-18
 - Resolution of symptoms
 - Resolution of leukocytosis and thrombocytosis
 - RNA present in stool for 64 days but no known transmission
- Death rate 9.6% but age >60 death rate 45%
- Children mostly spared

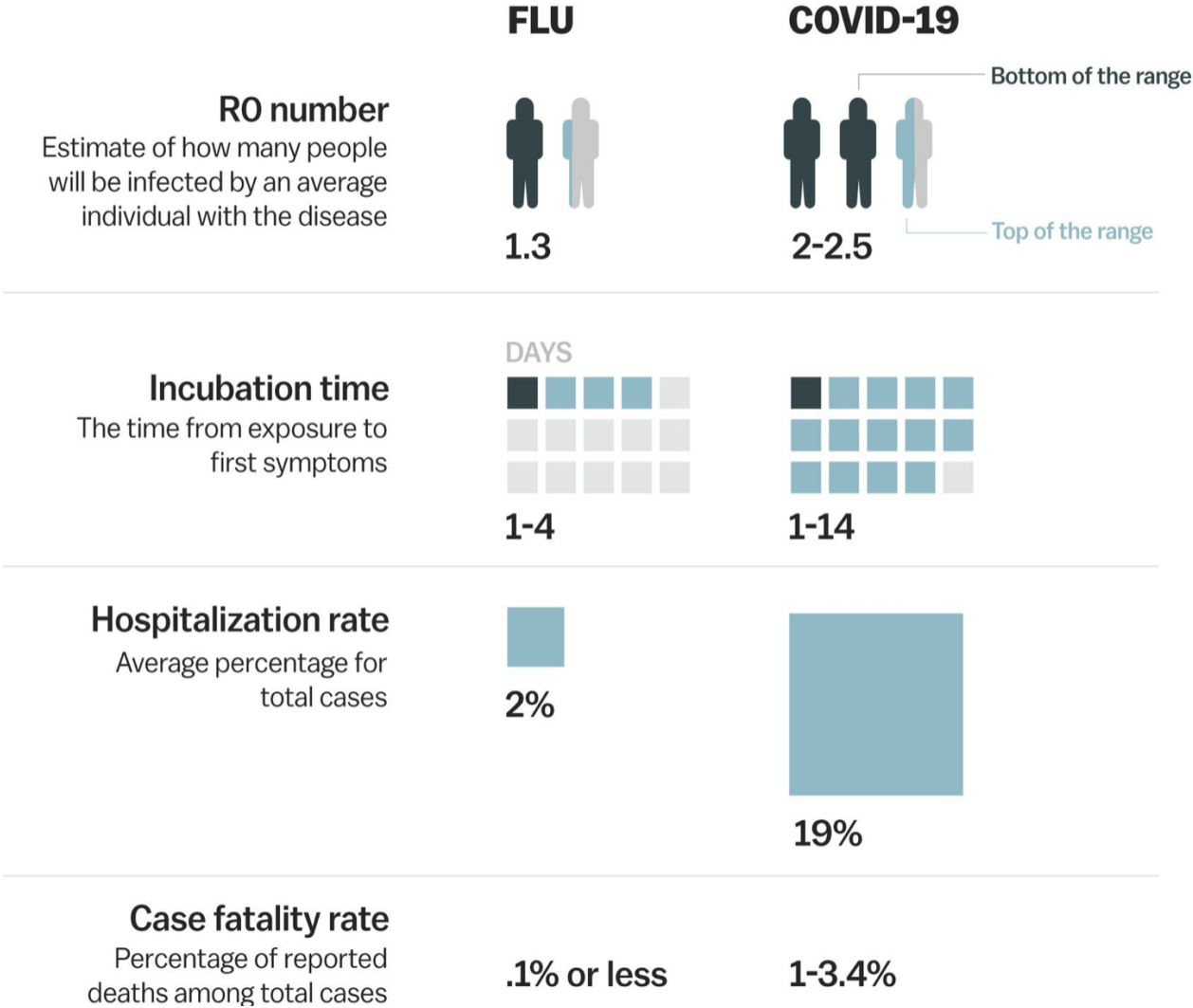
MERS-CoV: Middle East Respiratory Syndrome

- Saudi Arabia: 85.8% reported cases
- Camel to human transmission
 - Nasal secretions
 - Milk
 - Meat
- Presentation
 - Fever 98%
 - Cough 83%
 - URI: 70%
 - Lymphopenia 34%
 - Abnormal CXR: 100%
- Treatment: supportive
- Children mostly spared

COVID-19

- Wuhan China
- Infection vector: droplets, direct contact
- R0: Basic reproduction number 2.3% (95% CI 1.4-3.9)
- Symptoms
 - Fatigue, fever, dry cough, dyspnea, abdominal pain, anorexia
 - CT patchy shadows, ground glass appearance
- Progression
 - ARDS
- Treatment
 - Empiric, evolving
- Vaccine
 - ETA fall 2021

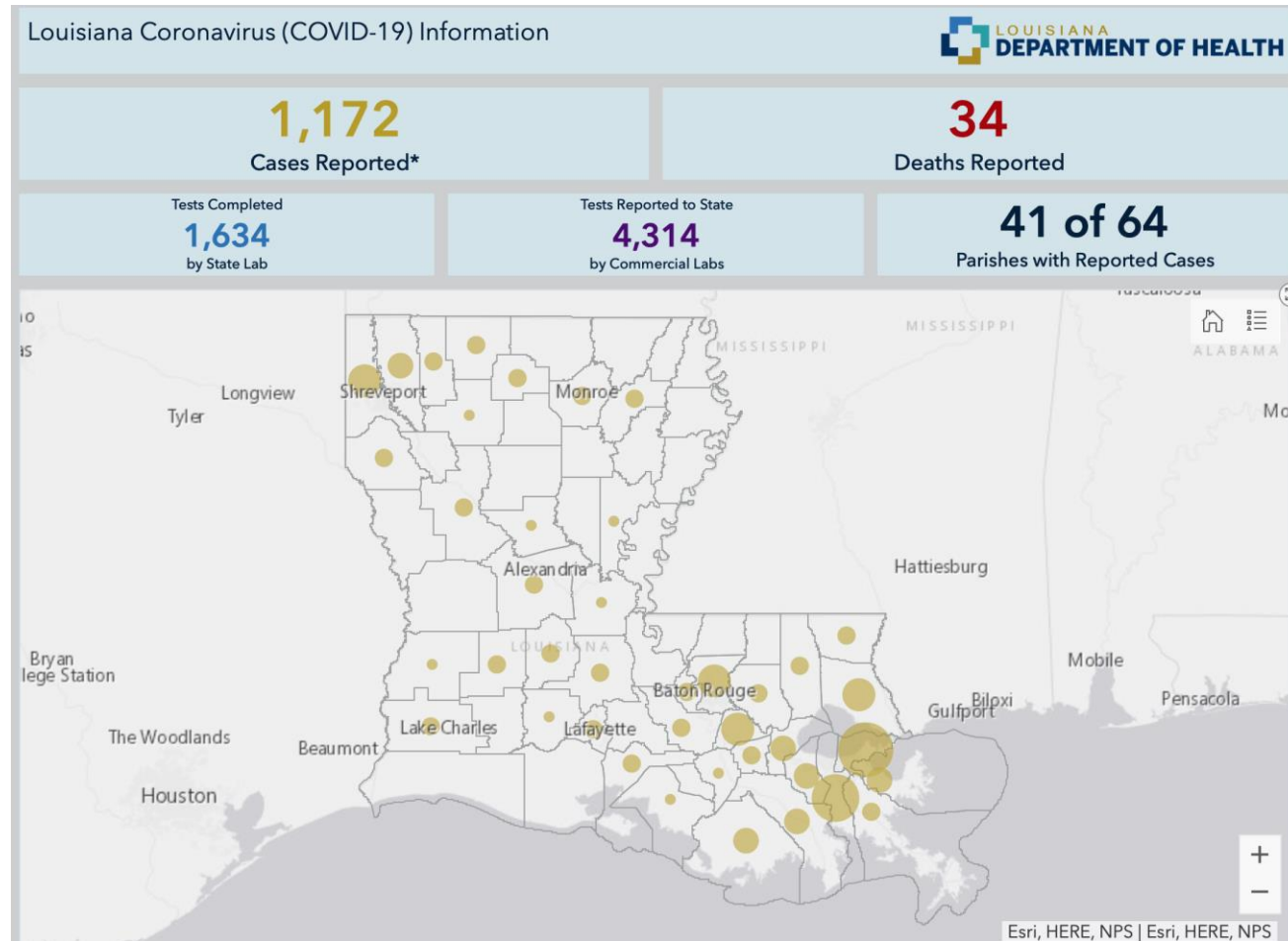
How seasonal flu and Covid-19 compare



COVID-19 Clinical Features

- Age distribution (N = 44 672)
 - 80 years: 3%(1408 cases)
 - 30-79 years: 87%(38 680 cases)
 - 20-29 years: 8%(3619 cases)
 - 10-19 years: 1% (549 cases)
 - 10 years: 1% (416 cases)
- Symptoms
 - Lymphopenia 83.2%
 - Dry cough 67.8%
 - Fatigue 70%
 - Fever 43.8% on admission 88.7% during hospitalization
 - Anorexia 40%
- Guan,W Clinical Characteristics of Coronavirus Disease 2019 in China NEJM Feb 28, 2020

COVID-19 in Louisiana 3/22/20



Clinical Characteristics of Coronavirus Disease 2019 in China

Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., Yu Hu, M.D., Wen-hua Liang, Ph.D., Chun-quan Ou, Ph.D., Jian-xing He, M.D., Lei Liu, M.D., Hong Shan, M.D., Chun-liang Lei, M.D., David S.C. Hui, M.D., Bin Du, M.D., Lan-juan Li, M.D., [et al.](#), for the China Medical Treatment Expert Group for Covid-19*

Lab	Change	Incidence ^{1,2}
Lymphopenia	<1500/mm ³	35-70%
Leukopenia	4.7 median	9-33.7%
Hematocrit	Decrease	41-50%
Thrombocytopenia	<150/mm ³	4-35%
AST/ALT	Increase	4-22%
LDH	Increase	27-75%
CRP	Increase	61-85
Procalcitonin	Can be > 0.5	5.5% 14% if severe 24% if ICU

COVID-19 Clinical Features cont.

Case-fatality rate

- 2.3%(1023 of 44 672 confirmed cases)
- 14.8%in patients aged 80 years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0%in critical cases (1023 of 2087)

Health care personnel infected

- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

Wu,Z Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China, JAMA Online published Feb 24, 2020

STAY HOME

**UNLESS YOU WANT TO
BE INTUBATED BY A
GYNECOLOGIST**

Severe COVID-19

- Prodrome 5-7 days
- Acute worsening
- Auto-immune
- ARDS
 - Conservative fluid strategies if no shock
 - Empiric early antibiotics, adjust with appropriate diagnosis
 - Lung-protective ventilation, avoid high pressure, high tidal volumes, oscillation
 - Prone positioning
 - Avoid bi-pap as it spreads virus
 - CDC cautions against corticosteroids as prolonged viral replication in MERS-CoV
- Guan,W Clinical Characteristics of Coronavirus Disease 2019 in China NEJM Feb 28, 2020

Severe COVID-19

- Etiology of severe disease
 - DIC
 - Septic Shock
 - Acute Kidney Injury
- Course for hospitalized patients
 - 32% severe pneumonia
 - 19% ARDS
 - 1.4-4.3% mortality (may decrease with testing of asymptomatic patients)
 - Most severe among elderly and those with significant medical comorbidities
- Guan,W Clinical Characteristics of Coronavirus Disease 2019 in China NEJM Feb 28, 2020

COVID-19 Mortality

- Cause of death
 - Progressive hypoxia
 - Multiorgan dysfunction
- Lab abnormalities
 - Lymphopenia worsening in non-survivors
 - D-dimer higher in non-survivors
 - Blood urea and creatinine increase prior to death
- Etiology
 - Cytokine storm
 - Coagulation activation
 - Myocardial, hepatic and kidney injury
 - Similar to MERS-CoV and SARS-CoV

• Guan,W Clinical Characteristics of Coronavirus Disease 2019 in China NEJM Feb 28, 2020

COVID-19 Mortality

Zhou F Yu T Du R et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020; (published online March 9.)

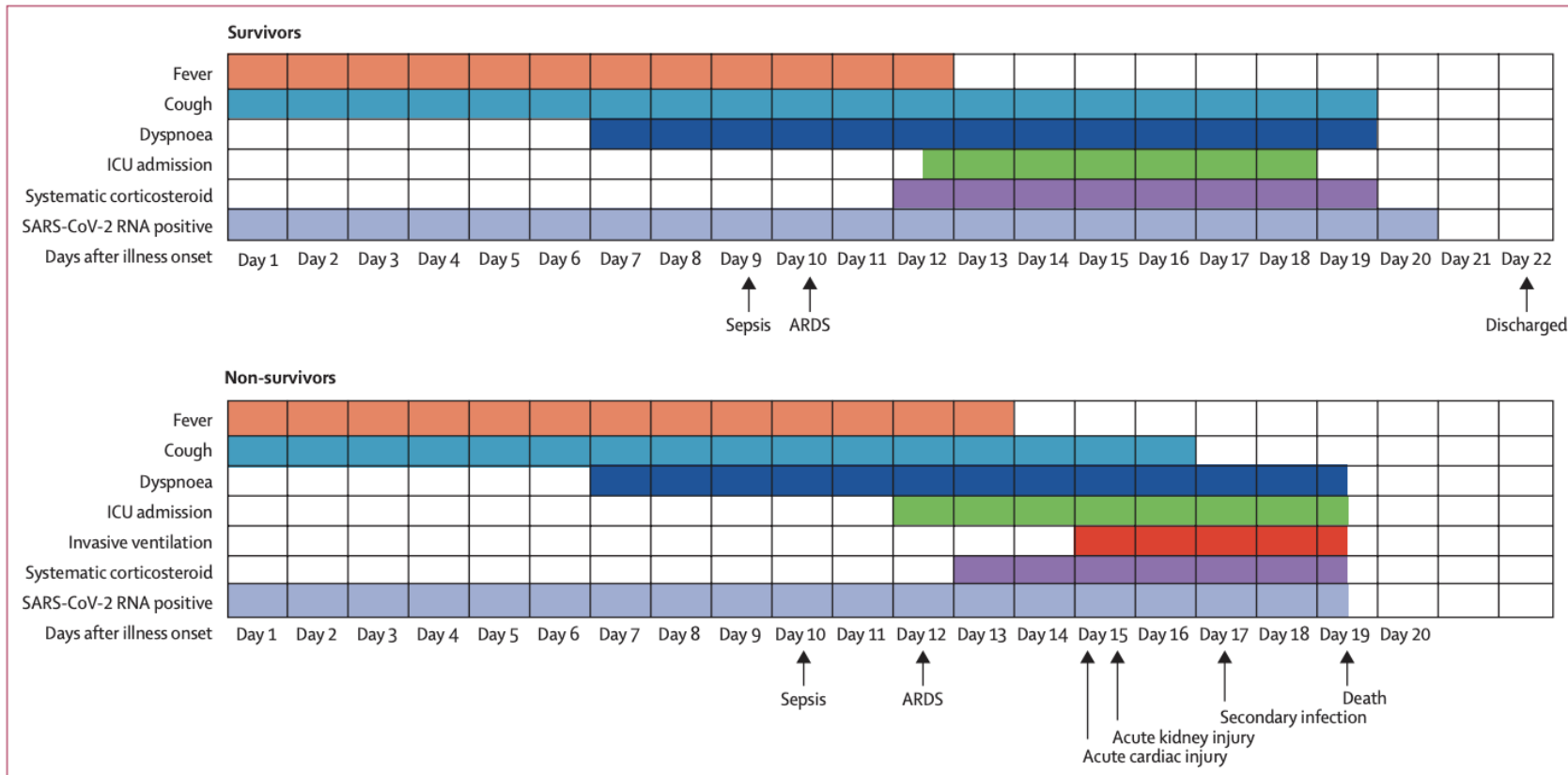
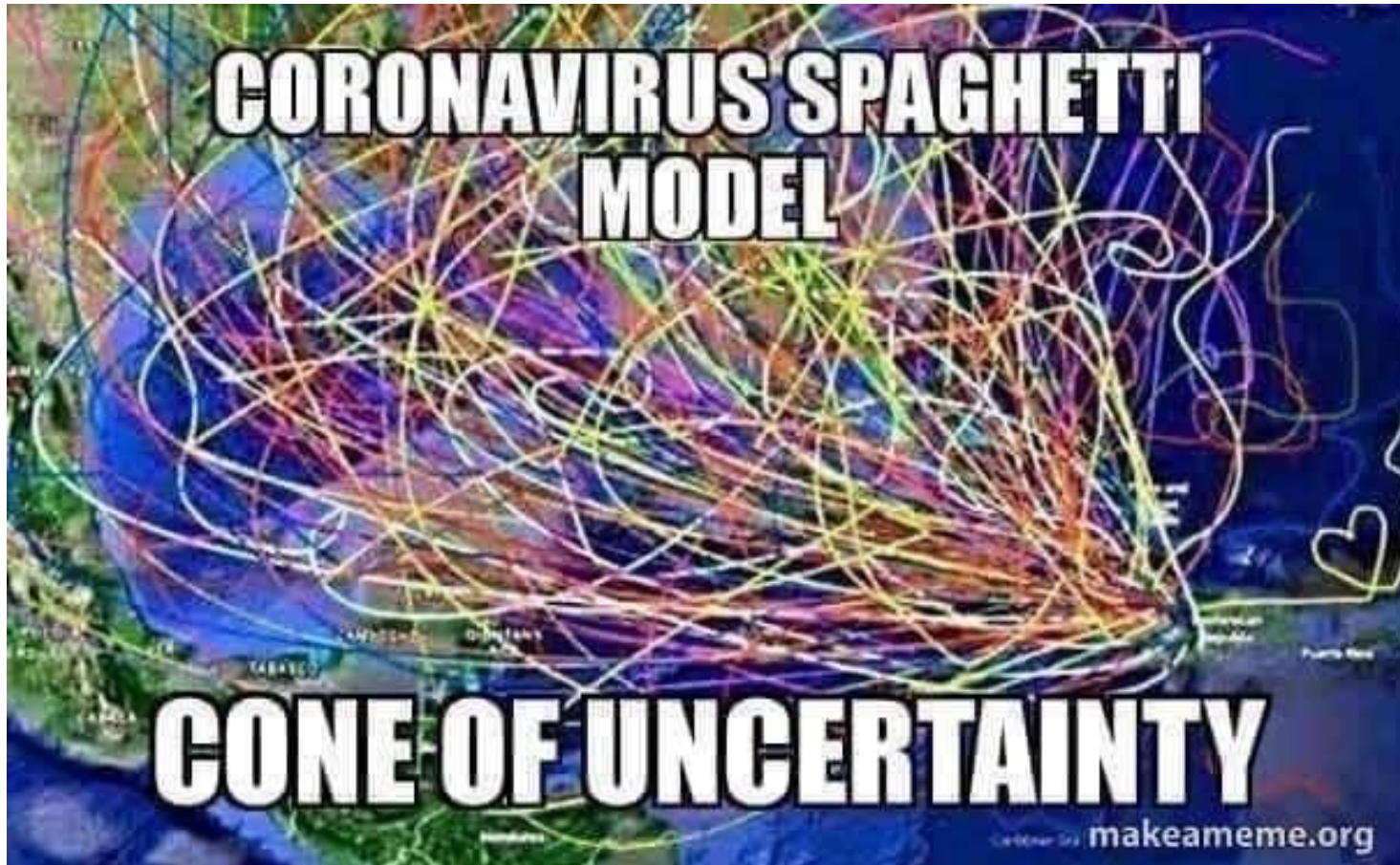


Figure 1: Clinical courses of major symptoms and outcomes and duration of viral shedding from illness onset in patients hospitalised with COVID-19

Figure shows median duration of symptoms and onset of complications and outcomes. ICU=intensive care unit. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ARDS=acute respiratory distress syndrome. COVID-19=coronavirus disease 2019.

Treatment: Dr. Anthony Fauci “anecdotal”



Remdesivir

- Not currently FDA approved, 5 clinical trials underway
- Analog to adenosine, inhibits RNA replication
- In-vitro activity against SARS-CoV-2 and in vivo activity against betacoronaviruses
- Shown safe in humans against Ebola
- Inhibits MERS in monkeys
- Not effective once auto-immune mechanism begins
- Pregnant women excluded from clinical trials
- Compassionate use

Hydroxychloroquine (Plaquenil)/Chloroquine

- Not currently FDA approved
- Anti-malarial and treatment of rheumatic disease, limits uptake of virus into cells?
- In vitro results in China encouraging
- Non-randomized un-blinded trial 24 patients Marseille France: reduced viral load
- Safe in pregnancy
- Dose: 400 mg BID for 2 doses then 200 mg BID for 8 doses
- Azithromycin?
- Prolonged QT interval

- Yao,X In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus-2 Clinical Infectious Diseases 09 March 2020
- www.youtube.com/watch?v=n4J8kydOvbc

Other potential therapies

- None FDA approved
 - Tocilizumab (Actembra): IL-6 inhibitor
 - Anti-Ebola medications: NHC, EIDD-2801, EIDD 1931
 - Lopinavir-ritonavir (Kaletra): combined protease inhibitor not effective
 - Corticosteroids: “Given the lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason.” IVIG from survivors
 - Anti-ACE2 receptor antibodies: do NOT stop ACE inhibitors
 - NSAIDS: upregulate ACE2 expression, consider other pain relief modalities for COVID if possible, FDA “investigating”
-
- Coa,B A Trial of Lopinavir-ritonavir in Adults Hospitalized with Severe Covid-19 NEJM March 2020
 - CDC Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected Interim guidance 13 March 2020

**This week y'all are
scared of Corona Virus,
last week you were
eatin Moonpies from the
gutter at Mardi Gras.**

COVID-19 in pregnancy

- 9 cases from China
- 1 woman required mechanical ventilation
- Preterm birth probably iatrogenic
- Cesarean delivery 100% (cultural?)
- No neonatal deaths, all infants reported “well”
- No vertical transmission
 - Amniotic fluid
 - Cord blood
 - Throat swab
 - Breast milk
- SARS, MERS and Flu all increase rate of low birth weight and preterm birth
- Chen,H et al Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records Lancet Feb 12, 2020

COVID-19 in Pregnancy

- 13 patients from China
- Presenting symptoms
 - Fever: 10 (77%)
 - Dyspnea: 3 (23%)
 - None: 1 (close contact)
- Disposition
 - Improved and discharged: 3 (23%)
 - Delivered: 10 (77%), , all by CD
 - ⦿ Emergent = 5; NRFHT = 3, PPRM = 1, IUFD = 1
 - Preterm labor 32-36 weeks = 6 (46%)
 - ICU admission = 1 ARDS/ventilation, acute hepatic failure, ARF, septic shock → ECMO
- No vertical transmission

Liu, Y Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy Journal of Infection Feb 27, 2020

Severe COVID-19 in Pregnancy

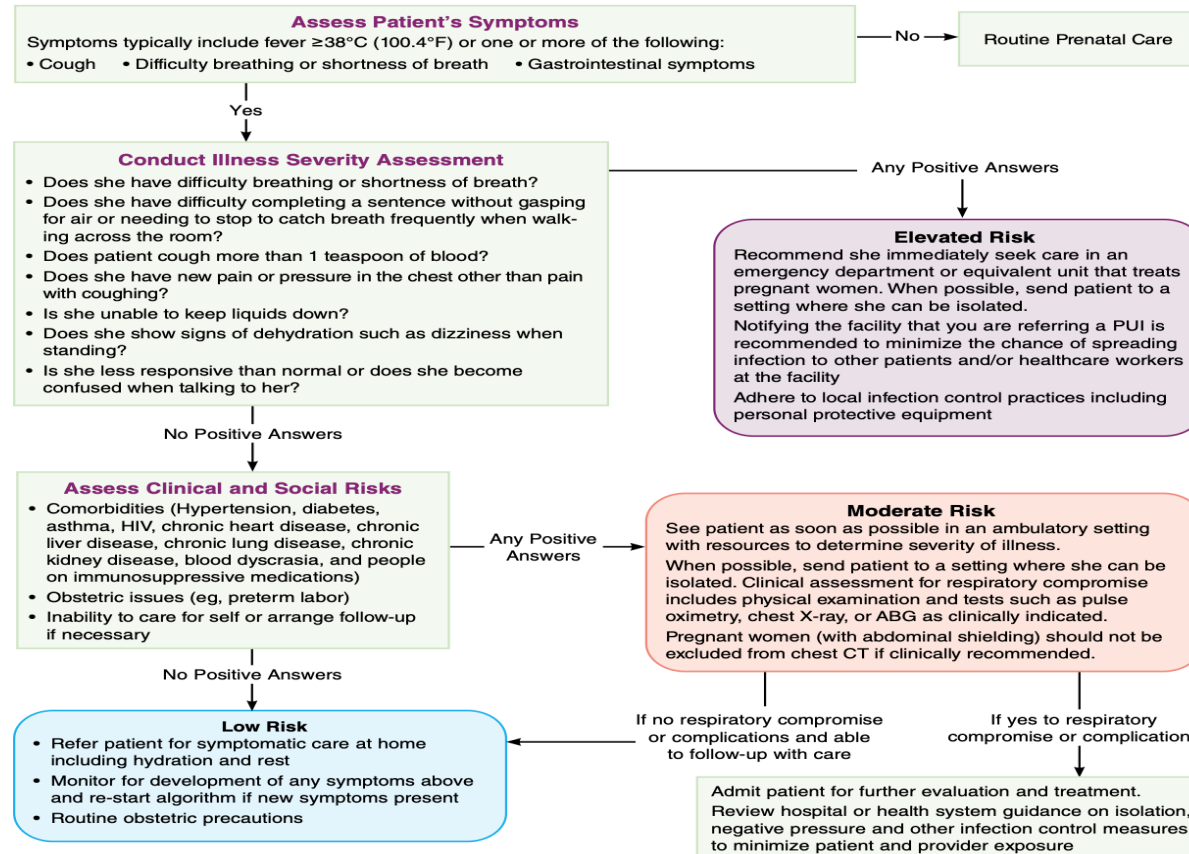
- Treat for optimal maternal health
 - CXR, CT if indicated
- Maintain oxygenation >92%
- Cautious use of corticoid steroids
 - No late-term steroids
 - Consult MFM if 24-34 weeks with COVID symptoms
- Positioning
 - Left decubitus positioning
- Broad spectrum antibiotics
- Consider off-label use of hydroxychloroquine
- Prophylaxis for VTE
- Continuous fetal monitoring
 - Only when delivery would not compromise maternal health
 - As “another non-invasive measure of maternal status”

SMFM webinar Han, Christina <https://education.smfm.org/products/covid-19-in-pregnancy-preparing-your-obstetrical-units>

COVID-19 in Pregnancy in Summary

- SARS, MERS and Influenza: worse outcomes in pregnant women
- COVID-19 available data are reassuring but are limited to small case series.
- Limited information about:
 - Susceptibility of pregnant women to COVID-19
 - Severity of infection
 - Data from the SARS epidemic are reassuring, suggesting no increased risk of fetal loss or congenital anomalies associated with infection early in pregnancy
- Denominator unknown
- Timing of delivery, in most cases, should not be dictated by maternal COVID-19
- Hughes, J Coronavirus (COVID-19) and Pregnancy: What Maternal-Fetal Medicine Subspecialists Need to Know SMFM
https://s3.amazonaws.com/cdn.smfm.org/media/2267/COVID19-_updated_3-17-20_PDF.pdf

ACOG/SMFM Algorithm



Abbreviations: ABG, arterial blood gases; CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus.
Healthcare providers should immediately notify their local or state health department in the event of a PUI for COVID-19 and should contact and consult with their local and/or state health department for recommendations on testing PUIs for COVID-19.

COVID-19 and Delivery

- No alteration in timing of delivery, not indication for delivery
- Reasonable to postpone delivery until negative test result or end of quarantine status
- Mode of delivery: usual obstetric practice
- Restrict visitors, providers
- Discharge planning includes in-home quarantine
- Discontinuation of in-home isolation
 - Resolution of fever x 3 days
 - Improved symptoms, 7 days from onset
 - 2 consecutive negative swabs >24 hours apart

COVID-19 and Newborn

- No clear evidence of vertical transmission to date (1 possible report)
- Youngest patient 36 hours old born by C/S (neonatal transmission)
- Current CDC guidelines:
 - separate rooms for confirmed or suspected infection in mother OR
 - 6 ft separation from mother +/- curtain
 - Hand hygiene, PPE for baby's caregiver
- Breastfeeding encouraged
 - Important to establish supply
 - Source of antibodies for infant
 - Careful cleaning of breast pump
 - Hand hygiene and face mask if putting baby to breast

Qiao, J Lancet Comment Feb 12, 2020

COVID-19 and Children

- 2143 cases <18 yo in China; 1/3 confirmed; 2/3 presumed
- Asymptomatic: 4%
- Mild symptoms: 50%
 - Fatigue, fever, cough, congestion
- Moderate symptoms: 39%
 - Pneumonia, SOB
- Severe symptoms: 6%
 - 60% <5 yo
 - 40% <12 months
- Etiology of milder course?
 - Less chronic lung damage, milder auto-immune response

Dong, Y Epidemiological Characteristics of 2143 Pediatric Patients with 2019 Coronavirus Disease in China, Pediatrics March 2020

**Corona Virus
Prevention: Wash your
hands like you gotta
take your contacts out
and you just finished
eating crawfish.**

COVID-19 Prevention in Pregnancy

- Waiting room well-ventilated area, > 6 feet from others
 - ⊙ Schedule to allow short wait
- Respiratory hygiene: Face mask on patient
- Rapid triage
 - ⊙ Separate OB ED from COVID Evaluation Unit
 - ⊙ Segregate providers if possible ie OB ED team, L+D team, postpartum team
- Isolated ASAP using CDC Infection prevention and control procedures
- Limit visitor and HCP access to patient rooms
 - ⊙ No visitors with outpatient visits
 - ⊙ 1 support person in labor
- Contact Hospital Infection Control

Who Should Be Tested?

Criteria for testing as of 3/14/20 (subject to change)

PRESENTATION/SYMPTOMS	SARS-CoV-2 TESTING RECOMMENDED?	CONSIDER FLU TESTING?
Asymptomatic	No	No
Community Patients + Symptoms ² (includes all clinics, urgent care)	ONLY IF RISK QUALIFIER PRESENT ¹	If in season
Emergency Room Patients + Symptoms ²	ONLY IF RISK QUALIFIER PRESENT ¹	If in season
Hospitalized Patients + Symptoms ²	Yes*	Yes
Any Pregnant or Increased Risk Patient + Symptoms ² (See <i>RISK QUALIFIER Definition</i>) ¹	Yes*	Yes

- 1. RISK QUALIFIER:** Healthcare workers with direct contact with confirmed/presumed positive COVID case or pregnant women or patients with immunocompromising conditions (such as receiving immunosuppressive medications, solid organ transplant, hemodialysis, chronic lung disease, active cancer, advanced HIV), or people living in communal settings (nursing facilities, shelters, etc.) or infants ≤ 10 weeks of age/adjusted gestational age.
- 2. Symptoms of acute viral respiratory infection (Cough or Shortness of breath, myalgias, etc.) AND Fever (Temp ≥100.4)**

COVID-19 Testing in Pregnancy

- Upper respiratory nasopharyngeal swab ONLY (Oropharyngeal less important; conserve supplies)
 - ⦿ Both nares, All the way back
- Sputum collection only for those with productive cough, no induced sputum
- Synthetic fiber swabs with plastic shafts.
- Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing
- Maintain proper infection control while collecting specimen
 - ⦿ N-95 respirator/surgical mask
 - ⦿ Eye protection, gown, gloves
- Place swabs immediately into sterile tubes containing 2-3 ml of viral transport media

www.CDC.gov/coronavirus/2019-ncov/lab/clinical-guidelines

COVID-19 Impact on Obstetric Appointments

- Telehealth
 - COVID-19 pregnancy hotline
 - Connected Mom
 - Telehealth visits
- Ultrasound, antenatal surveillance and lab assessments
- High-risk conditions
- Social distancing
 - Waiting area
 - Called in from car
- Postpartum follow up, facilitating immediate post-placental LARC

Pregnant Healthcare Personnel

- May continue to work
 - If staffing allows, limit exposure to confirmed or suspected cases
- Standard PPE including N-95 and eye protection
- If possible, avoid high-risk procedures
 - Aerosol-generating procedures such as nebulizers
 - Intubation and extubation
 - CPR
- Also applies to those at risk for severe complication from infection
 - >age 70
 - Chronic medical conditions (lung disease, heart disease, diabetes)
 - Immunocompromised

Proper Personal Protective Equipment

https://www.nytimes.com/2020/03/13/world/how-to-wash-your-hands-coronavirus.html?te=1&nl=well&emc=edit_hh_20200319&campaign_id=18&instance_id=16881&segment_id=22370&user_id=18899ee31df58feb08db4209a65cb2aa&egi_id=6678033120200319

Kill Germs The Cajun Way

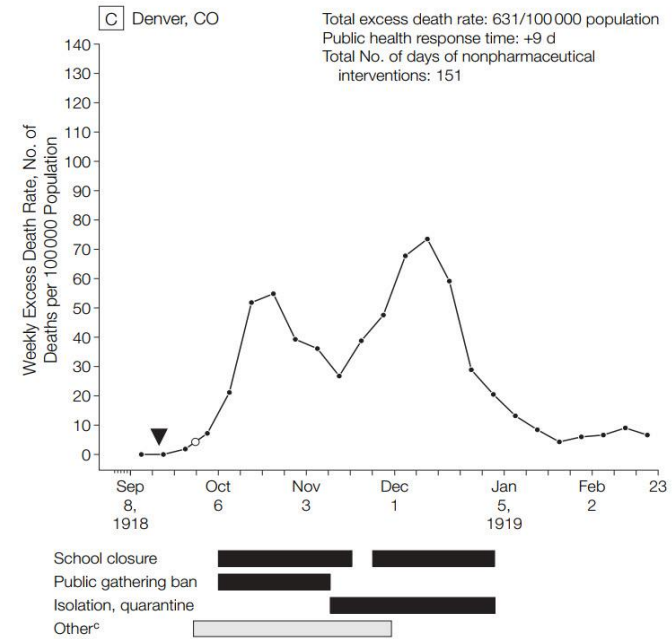
NEW



Not only does it kill germs, it also prevents you from sticking your fingers in your eyes, nose, and mouth (and other places) **a second time**

COVID-19 and our Future

- Flattened curves but subsequent waves
- Recurrence with re-emergence
 - Denver flu
 - SARS
- Successful social distancing means fewer immune people
- Vaccine not effective until 45-70% of population vaccinated
- “We are actively redesigning the way we deliver care to do what is best for our patients during this time of crisis. Some aspects of that redesign will likely persist after the crisis has passed.”
- Lee, T Creating the New Normal: The Clinician Response to Covid-19 NEJM March 17 2020



Dear Netflix,

Can you please turn off the “are you still watching” feature? We are in quarantine so yes we are still watching, I don’t need this kind of judgment in this time of uncertainty. If you could please update it with a “are you sure you want to eat that” notice that would be much more helpful at this time.

Patient resources

- Ochsner: <https://www.ochsner.org/coronavirus>
- Up To Date: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-the-basics?search=covid-19-2019-novel-coronavirus-the-basics&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3
- HUHS: <https://huhs.harvard.edu/about-us/announcements-events/coronavirus-information-and-updates>
- CDC pregnancy: <https://www.cdc.gov/coronavirus/2019-ncov/specific-groups/pregnant-women-and-children.html>

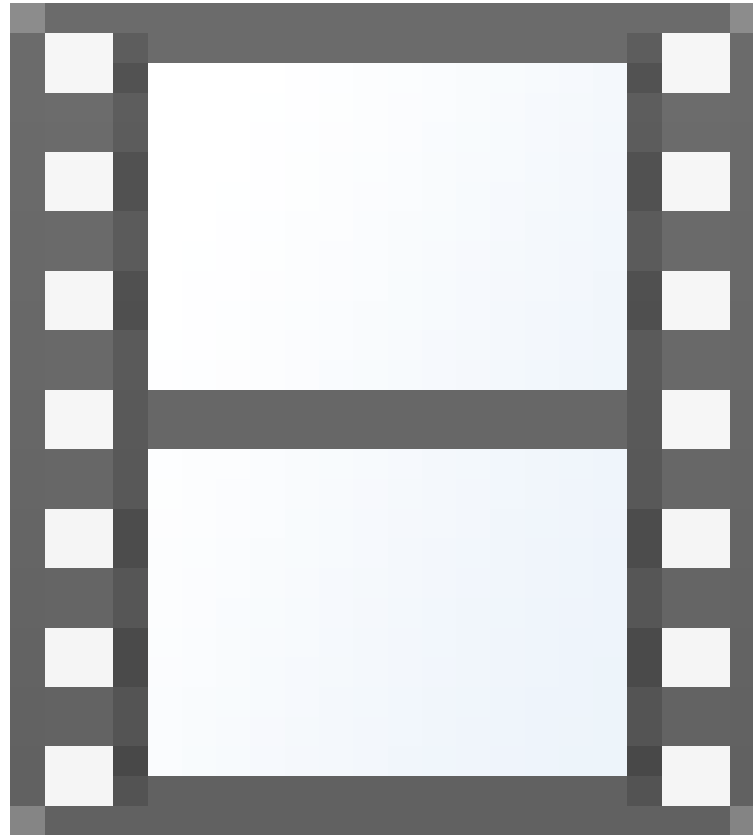
CDC Resources: Rapidly changing landscape!!

- Infection prevention (<https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-recommendations.html>)
- Inpatient management and breastfeeding (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html>).
- Testing guidelines (<https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>).
- Travel guidelines (<https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html>).

Additional resources

- Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. Am J Obstet Gynecol 2020 Feb 24.
- CMQCC: <https://www.cmqcc.org/news/webinar-recording-preparing-your-maternal-and-neonatal-units-respond-covid-19>WHO: Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is expected: Interim guidance V 1.2
- SMFM: <https://youtu.be/fT5h4oMUOFk>
- ACOG: <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019>

Reality of Quarantine



Questions?

NOLA gonna NOLA



@drdaddyzwhodat