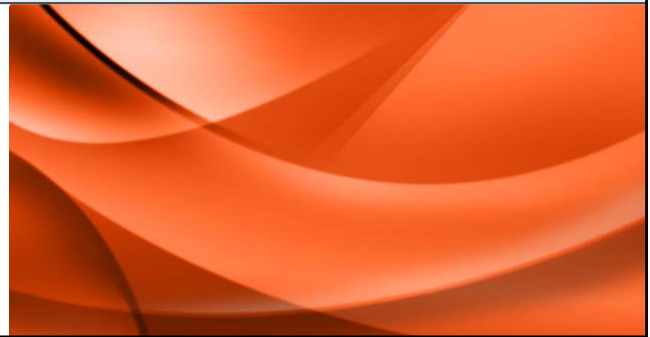




COVID-19: Basics and What We Know in HHT

Justin McWilliams, MD
Director, UCLA HHT Center of Excellence



Disclaimers:

I am an HHT physician



I am not a virologist, epidemiologist, or infectious disease physician

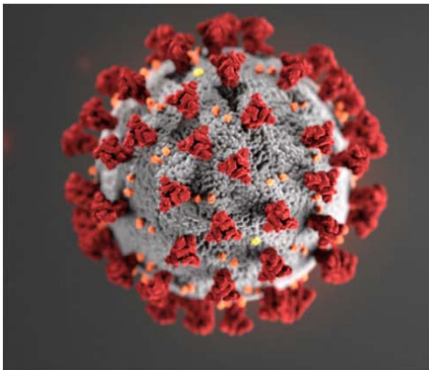
Much of the data we have is early, anecdotal, or based on personal/shared experiences, and may change over time.

Please consult with your HHT physician and/or primary care physician

COVID-19 Basics



What is SARS-CoV-2?



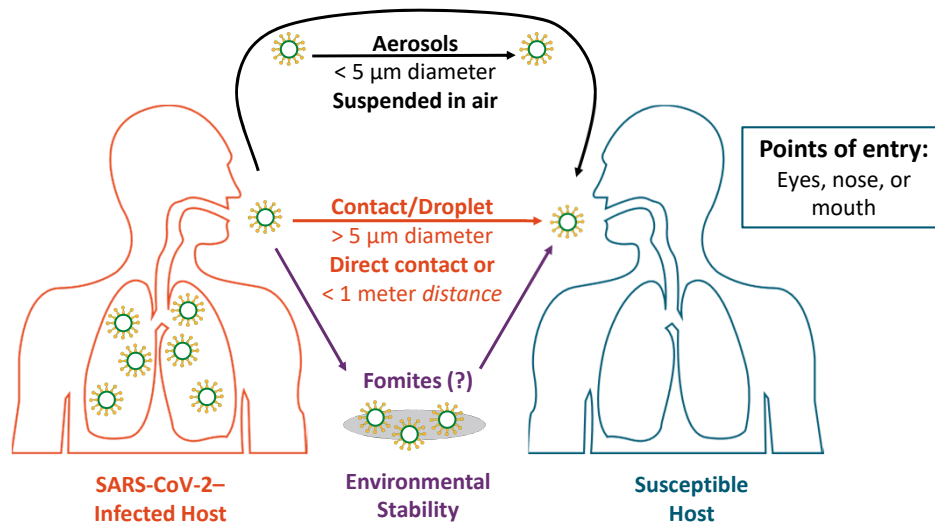
SARS-CoV-2 is the virus that causes coronavirus disease 2019 (COVID-19)

- SARS = severe acute respiratory distress syndrome
- Spreads easily person-to-person
- Little if any immunity in humans

Detailed information:

<https://www.cdc.gov/coronavirus/2019-ncov/index.html>

Routes of SARS-CoV-2 Transmission



Galbadage. Front Public Health. 2020;8:163. WHO. Scientific Brief. July 9, 2020.

Slide credit: clinicaloptions.com

The more people you
interact with...

The closer you
interact with them...

The longer the
interaction...

The higher the risk!

Global COVID-19 Dashboard



Confirmed Cases
Global: 75,334,482

- US: 17,326,926
- India: 9,979,447
- Brazil: 7,110,434
- Russia: 2,764,843
- France: 2,483,661

Deaths
Global: 1,669,577

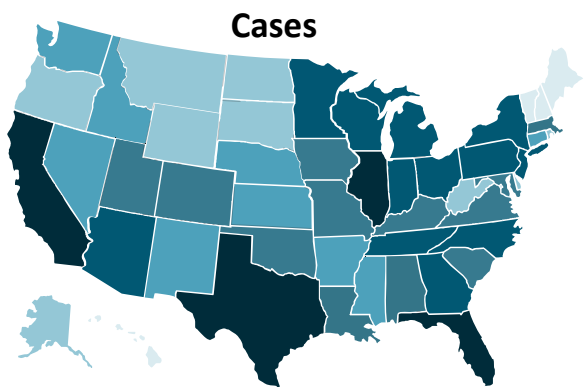
- US: 312,219
- Brazil: 184,827
- India: 144,789
- Mexico: 116,487
- Italy: 67,894

Last updated: December 18, 2020, 3:12 PM ET

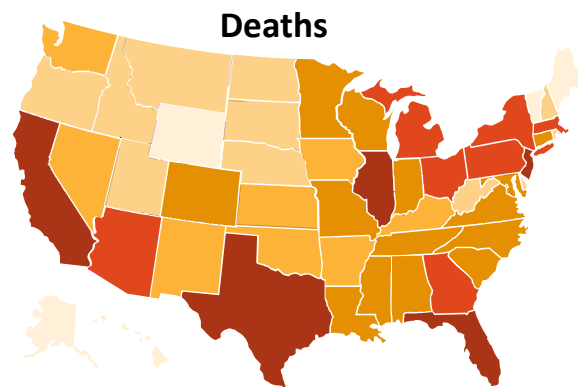
Dong. Lancet Infect Dis. 2020;20:533. <https://coronavirus.jhu.edu/map.html>

Slide credit: clinicaloptions.com

CDC: US COVID-19 Tracker



0-31,875 121,299-203,797 368,187-570,602
 39,775-95,010 224,890-347,603 856,118-1,585,044



0-321 1978-3273 7358-12,620
 604-1555 3969-6845 15,455-24,561

Last updated: December 15, 2020 12:17 PM ET

<https://www.cdc.gov/covid-data-tracker>

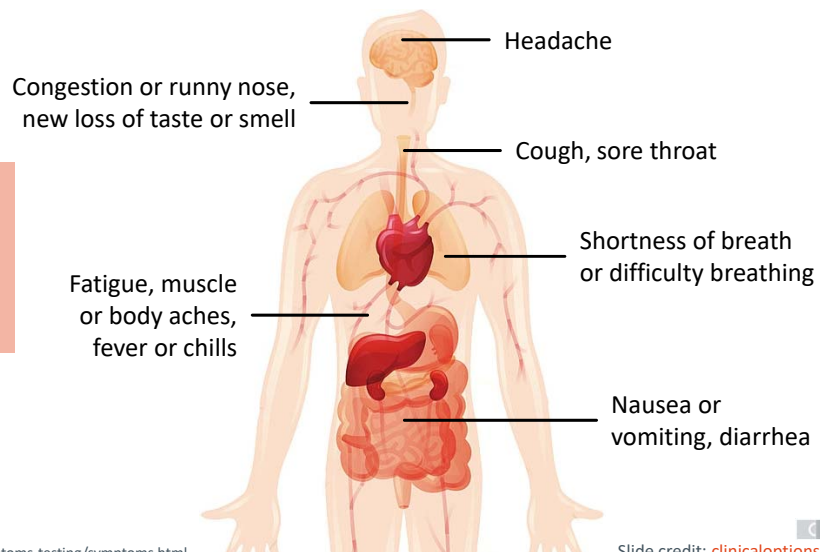
Slide credit: clinicaloptions.com

Incubation period

- The incubation period is the time between exposure to a virus and the onset of symptoms.
- With COVID-19, symptoms may show 2-14 days after exposure.
- CDC indicates that people are most contagious when they are the most symptomatic.
- People may be contagious before developing symptoms.

Primary Symptoms of COVID-19

“Symptoms may appear **2-14 days** after exposure to the virus”



Li. J Med Virol. 2020;92:577.
<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

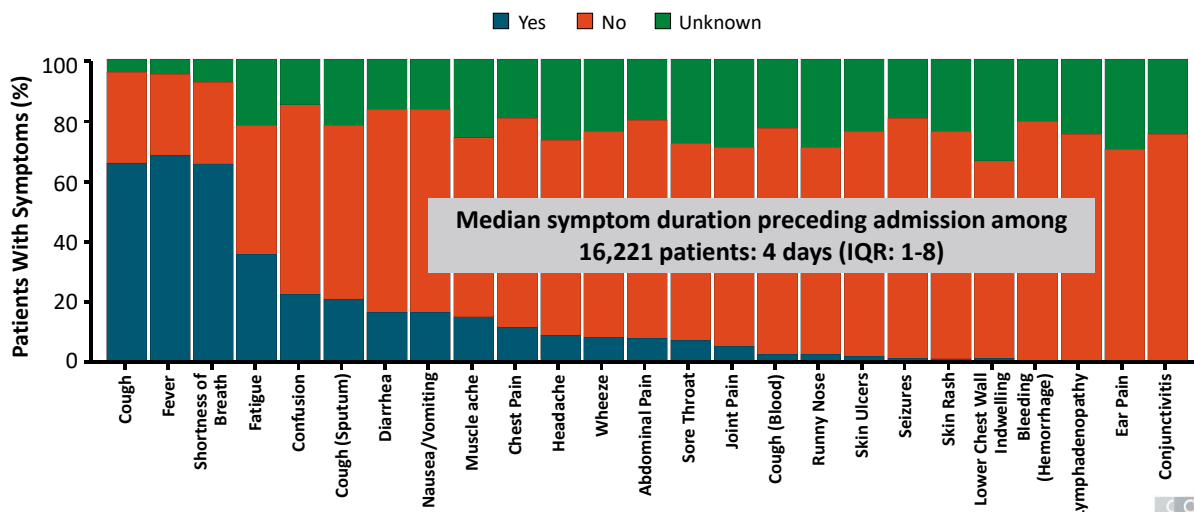
Slide credit: clinicaloptions.com

Severe symptoms – emergency warning signs for COVID-19

- Most people will have mild symptoms and should recover at home and **NOT** go to the hospital or emergency room.
- Get medical attention immediately if you have:
 - Difficulty breathing or shortness of breath.
 - Persistent pain or pressure in the chest.
 - New confusion or inability to arouse.
 - Bluish lips or face.



Frequency of Presenting Symptoms Among COVID-19-Positive Hospitalized Patients in the UK



Docherty. BMJ. 2020;369:m1985.

Slide credit: clinicaloptions.com

Seasonal flu vs. COVID-19

- SARS-CoV-2 is more infectious and spreads faster than the seasonal flu
- So far, the case fatality rate of COVID-19 is estimated to be around 2%.
- The case fatality rate of influenza is estimated to be around 0.1%, making SARS-CoV-2 about 20 times more deadly than the seasonal flu.
- An estimated 15-20% of COVID-infected individuals may suffer from severe symptoms that require medical attention, including pneumonia with shortness of breath and lowered blood oxygen saturation.

Preventative Interventions

Recommended Prevention Strategies^[1,2]

Identify and quickly test suspect cases with subsequent isolation of infected individuals

Quarantine close contacts of infected individuals

Wash hands often with soap and water

Maintain social distance (~ 6 feet)

Wear cloth face cover in public^[3,4]

Practice respiratory etiquette

Disinfect frequent-touch surfaces regularly

Avoid crowds, close-contact settings, and poorly ventilated spaces

1. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html> 2. WHO. Scientific Brief. July 9, 2020.
3. Leung. Nat Med. 2020;26:676. 4. Chu. Lancet. 2020;395:1973. 5. Kampf. J Hosp Infect. 2020;104:246.

Efficacy of Face Coverings in Prevention of SARS-CoV-2 Transmission

- Systematic review and meta-analysis of data from 172 studies investigating the spread of SARS-CoV-2, SARS, and MERS (n = 2647)^[1]
 - Face mask use (surgical, N95, or cotton mask) resulted **in large reduction in infection (OR: 0.15; 95% CI: 0.07-0.34)**
 - Association was stronger for N95 or respirators vs disposable or 12-16 layer cotton masks ($P_{\text{interaction}} = 0.090$)

1. Chu. Lancet. 2020;395:1973. 2. Leung. Nature Medicine. 2020;26:676.

Slide credit:  clinicaloptions.com

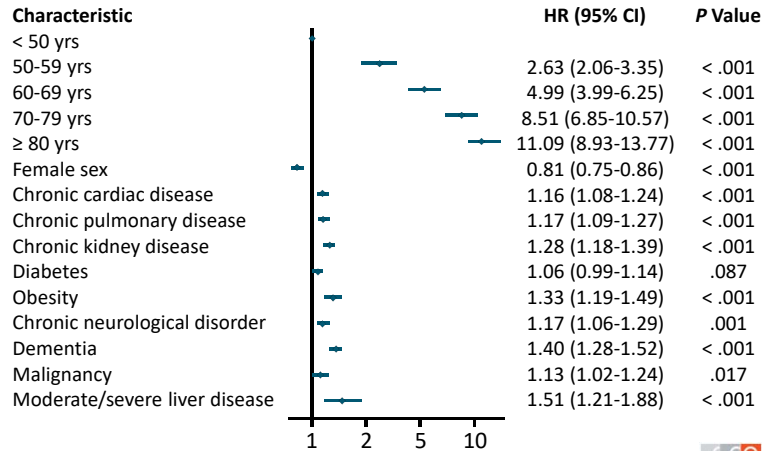
What We Know about COVID in Other Conditions



Predictors of Mortality Among COVID-19–Positive Hospitalized Patients in the UK

- Prospective observational cohort study of hospital admissions in England, Wales, and Scotland during February 6 - April 19, 2020 (N = 20,133)
 - Significantly increased risk of mortality among **older patients, men, and those with chronic comorbidities**

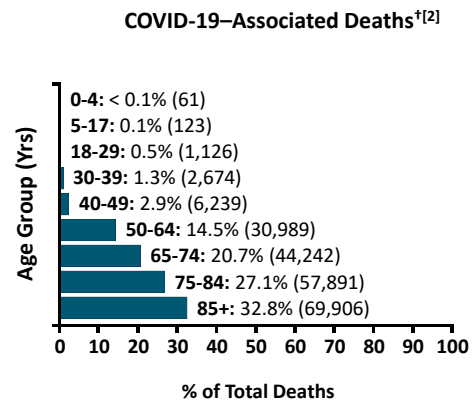
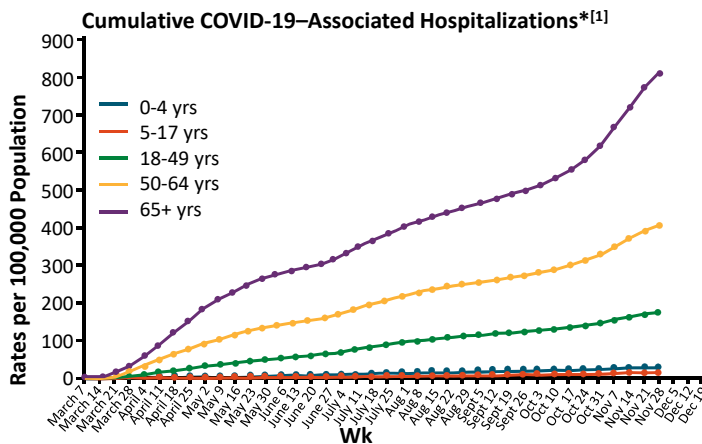
Multivariate Survival Analysis



Docherty. *BMJ*. 2020;369:m1985.

Slide credit: clinicaloptions.com

COVID-19–Associated Hospitalization and Death Rates Increase With Age in US



*Lab-confirmed COVID-19 cases; covers ~ 10% of US population: 99 counties in 14 states (CA, CO, CT, GA, IA, MD, MI, MN, NM, NY, OH, OR, TN, UT).

†Data from 213,269 deaths in confirmed and probable COVID-19 cases as reported by US states and territories; age group data available for 213,251 deaths (99%).

1. https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html
 2. <https://www.cdc.gov/covid-data-tracker/index.html#demographics>.

Slide credit: clinicaloptions.com

What We Know about COVID in HHT



PubMed.gov

Search: covid hereditary hemorrhagic telangiectasia

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RESULTS BY YEAR

TEXT AVAILABILITY

- Abstract
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- Full text

ARTICLE ATTRIBUTE

- Associated data

ARTICLE TYPE

- Books and Documents
- Clinical Trial
- Meta-Analysis
- Randomized Controlled Trial
- Review
- Systematic Review

PUBLICATION DATE

1 **Hereditary hemorrhagic telangiectasia and COVID-19.**
Mariano RZ, Pereira MC, Reis F.
Cite Rev Soc Bras Med Trop. 2020 Nov 25;53:e20200785. doi: 10.1590/0037-8682-0785-2020. eCollection 2020.
Share PMID: 33263694 Free PMC article. No abstract available.

2 **Angiogenesis, hereditary hemorrhagic telangiectasia and COVID-19.**
Riera-Mestre A, Iriarte A, Moreno M, Del Castillo R, López-Wolf D.
Cite Angiogenesis. 2020 Oct 14:1-3. doi: 10.1007/s10456-020-09755-5. Online ahead of print.
Share PMID: 33052496 Free PMC article.

3 **Hereditary haemorrhagic telangiectasia: A disease not to be forgotten during the COVID-19 pandemic.**
Gaetani E, Passali GC, Riccioni ME, Tortora A, Pola R, Costamagna G, Gasbarrini A; Multidisciplinary Gemelli Group for HHT.
Cite J Thromb Haemost. 2020 Jul;19(7):1799-1801. doi: 10.1111/jth.14885.
Share PMID: 32348627 No abstract available.

4 **Mental health and counseling intervention for hereditary hemorrhagic telangiectasia (HHT) during the COVID-19 pandemic: perspectives from Italy.**
Marano G, Gaetani E, Gasbarrini A, Janiri L, Sani G, Mazza M, Multidisciplinary Gemelli Group for HHT.
Cite Eur Rev Med Pharmacol Sci. 2020 Oct;24(119):10225-10227. doi: 10.26355/eurev.202010.23246.
Share PMID: 33090433 Free article.

5 **Diagnostic testing for SARS-CoV-2 infection in HHT patients: nasopharyngeal versus oropharyngeal swab.**
Pagella F, Lizzio R, Ugolini S, Spinazzi G, Maiorano E, Suppressa P, Sabbà C, Matti E.
Cite

Brazilian case report of 65 year old woman with HHT and low baseline oxygen levels with COVID-19. Eventual respiratory failure and death

Population study from Spain. HHT patients seem at similar risk from COVID-19 overall.

Letter to the Editor (opinion) of potential risks of COVID-19 in HHT

Experience from Italy showing loneliness and decreased mood of HHT patients in the face of the COVID-19 pandemic. Suggested web-mediated counseling for affected persons.

Experience from Italy suggesting fairly similar accuracy rates and less morbidity for oral / saliva COVID-19 test, recommended when possible

COVID-19 in HHT

- Little is known about COVID-19 in rare diseases
- Reasons for possible concern:
 - HHT patients often need to seek in-person medical care
 - Frequent touching of nose due to nosebleeds
 - Nasopharyngeal swabs for testing can provoke nosebleeds
 - HHT-related medical conditions may negatively influence the course of COVID-19
 - Chronic anemia
 - Heart failure
 - Pulmonary AVMs (from low oxygen levels)
 - Pulmonary hypertension

COVID-19 in HHT

- Reasons for possible concern (continued):
 - Increased clotting risk from COVID-19 may be particularly harmful in HHT
 - Treatments used in HHT may affect clotting risk
 - Tamoxifen
 - Avastin
 - Amicar/Tranexamic acid
 - Blood thinner treatments may not be tolerated in HHT patients
 - Psychological impact
 - Decreased mood / depression

COVID-19 in HHT

- Concern: HHT patients often need to seek in-person medical care

- Solutions:
 - Video or telephone visits with physicians
 - Delay elective tests or procedures
 - At-home management of nosebleeds whenever possible

COVID-19 in HHT

- Concern: Frequent touching of nose may increase COVID-19 exposure

- Solutions:
 - Practice good hand hygiene prior to touching nose
 - Frequent hand-washing or hand sanitizer

COVID-19 in HHT

- Concern: Nasopharyngeal swab testing may provoke nosebleeds
- Solutions:
 - Only test when advised to do so by your physician
 - Request oral swab / saliva testing when possible

Pagella et al. *Orphanet J Rare Dis* (2020) 15:350
<https://doi.org/10.1186/s13023-020-01428-w>

Orphanet Journal of
Rare Diseases

LETTER TO THE EDITOR

Open Access

Diagnostic testing for SARS-CoV-2 infection in HHT patients: nasopharyngeal versus oropharyngeal swab

Fabio Pagella^{1,2}, Roberta Lizzio¹, Sara Ugolini^{1,2}, Giuseppe Spinozzi¹, Eugenia Maiorano^{1,2}, Patrizia Suppressal¹, Carlo Sabbà³ and Elina Matti¹



COVID-19 in HHT

- Concern: HHT-related medical conditions may worsen the course of COVID-19
- Solutions:

The CDC has recommended that patients with significant underlying illnesses receive the vaccine earlier during initial distribution. While HHT is a chronic disease, the committee feels that the diagnosis of HHT by itself would not place a patient at an increased risk for severe illness. However, there are some patients with HHT and associated co-morbidities that should be considered higher risk and therefore placed into the pool of people to be vaccinated earlier. These would include:

- Patients with **heart failure**
- Patients with **Pulmonary Arterial Hypertension**
- Patients with **Pulmonary AVMs** who experience chronic low blood oxygen levels (Pulse oximetry < 90%)
- **Patients with HHT who frequently access the health care system** which may include those receiving frequent iron infusions, blood transfusions or bevacizumab treatments.

COVID-19 in HHT

- Concern: Increased clotting risk with COVID-19 may be particularly harmful in HHT
 - Passage of clot through untreated PAVM could cause TIA or stroke

- Solutions:
 - Individual assessment of risk vs benefit
 - Pulmonary AVMs of significant size should be embolized
 - HHT patients hospitalized with COVID-19 should receive standard of care therapies

COVID-19 in HHT

- Concern: Treatments used in HHT may affect clotting risk

- Solutions:
 - May temporarily stop certain HHT treatments if diagnosed with COVID-19
 - Discuss with your physician

COVID-19 in HHT

- Concern: Psychological impact of HHT

- Solutions:
 - Distance does not always mean isolation
 - Maintain close contact with family and friends (Zoom, FaceTime, etc)
 - Web-mediated counseling

Angiogenesis
<https://doi.org/10.1007/s10456-020-09755-5>

LETTER



Angiogenesis, hereditary hemorrhagic telangiectasia and COVID-19

Antoni Riera-Mestre^{1,2,3} · Adriana Iriarte^{1,3} · Manuela Moreno^{3,4} · Raul del Castillo^{3,5} · Daniel López-Wolf^{3,6}

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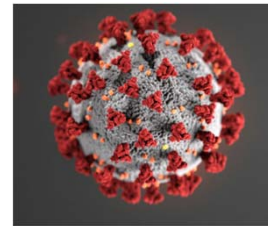
- Survey of 22 Spanish hospitals contributing to an HHT registry in June 2020
- Total of 1177 HHT patients followed by investigators at these sites
- Only 1 patient out of 1177 (74 yo woman) admitted with COVID-19 pneumonia
 - Recovered well and discharged after 2 weeks
- Why so few HHT patients with COVID-19?
 - More strict self-isolation?
 - Other effect?

COVID-19 in HHT: Site survey

- Recent survey of the site directors at 14 HHT Centers of Excellence across North America and Europe
- About 40 total cases of COVID-19 in HHT patients reported to the site directors
 - Out of thousands of patients (some patients may not have reported their COVID infection)
 - Most cases were mild
 - One MI, one small stroke
 - Two COVID-19 related deaths (both in patients with multiple other medical conditions)
 - In patients with known PAVM, course seemed similar to non-PAVM patients (mostly mild, a few more severe with low blood oxygen)
 - No DVT or PE
- Observational data is not showing increased risk of COVID-19 in HHT patients

Conclusions

- COVID-19 is highly infective, easily spread, and has a widely variable clinical course
 - Fever, cough, shortness of breath, loss of smell/taste
 - Most cases are mild
 - A minority require hospitalization
 - About 2% of cases are fatal (age is greatest risk factor)
- Wear a mask, socially distance, avoid indoor gatherings, wash hands
- HHT patients seem to be equally affected as the general population
 - Certain subgroups may be higher risk



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December CDC Update

- Conditions which increase risk of severe illness from COVID-19:
 - Cancer
 - Chronic kidney disease
 - COPD
 - Down syndrome
 - Heart conditions including heart failure
 - Organ transplant recipients
 - Obesity
 - Pregnancy
 - Smoking
 - Type 2 Diabetes

December CDC Update

- Conditions which *might* increase risk of severe illness from COVID-19:
 - Asthma (moderate to severe)
 - Cerebrovascular disease
 - Cystic fibrosis
 - Hypertension
 - Immunocompromised state
 - Neurologic conditions such as dementia
 - Liver disease
 - Overweight
 - Pulmonary fibrosis
 - Type 1 Diabetes