Long Term Care ASIC Call
May 5, 2020

Tennessee Department of Health
Healthcare Associated Infections and Antimicrobial Resistance Program

Welcome

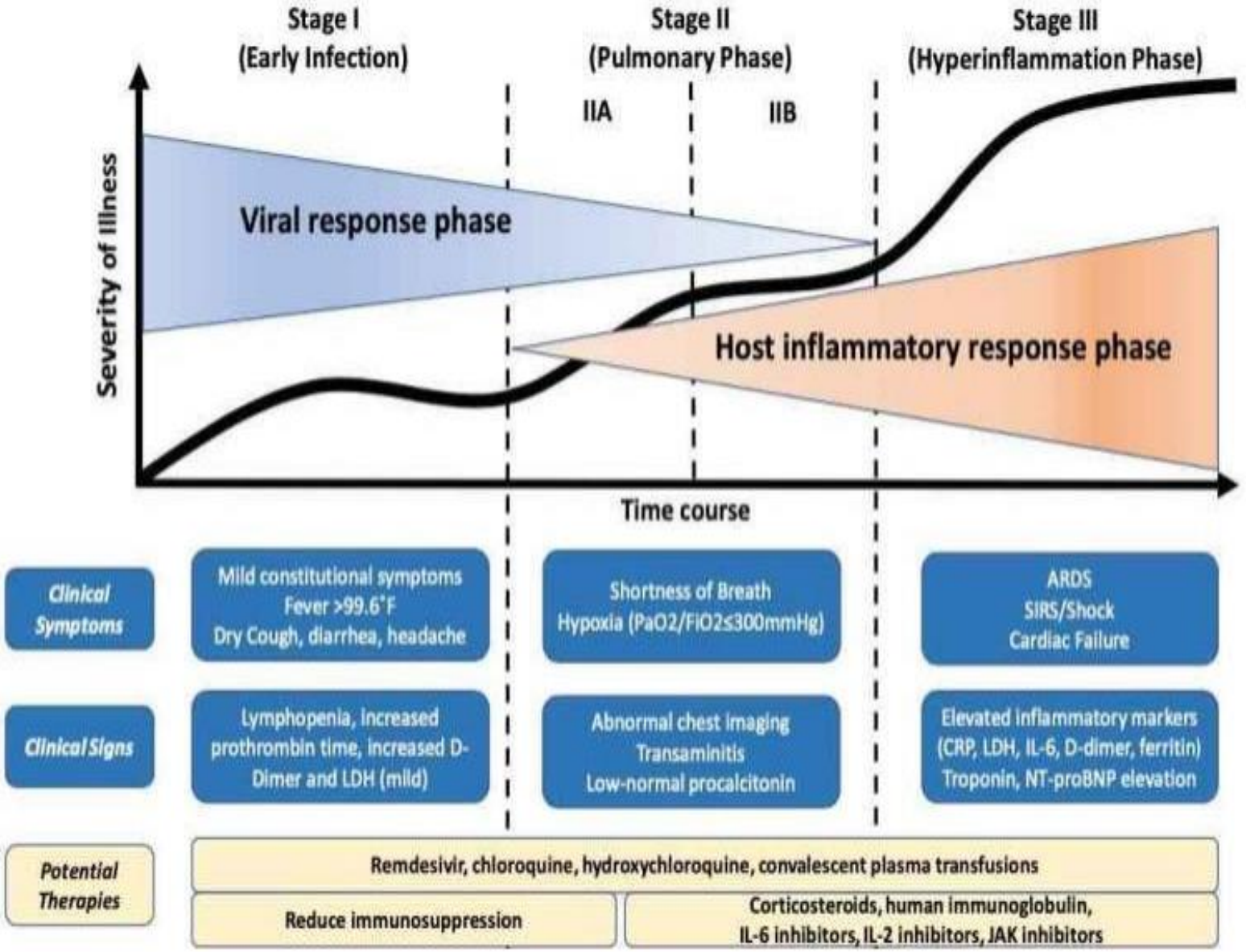
Agenda

- **Potential COVID-19 Treatment Options**
- **Announcements**

COVID-19 Treatment

First…a disclaimer

- **There are NO antiviral drugs proven to work against COVID-19 in humans**
  - **RCT ongoing**
- **There are no drugs currently approved by the FDA to prevent or treat COVID-19**



Slide Courtesy of M. Green

Hydroxychloroquine and Chloroquine

- **Increases endosomal pH of virus and interferes with glycosylation of cellular receptors**
- **In vitro studies show activity at both entry and post-entry stages of infection**
- **FDA issued Emergency Use Authorization for use against COVID-19 on March 28**
- **Liver, ocular, and cardiac toxicity**
  - **Prolongs QT interval**
  - **HCQ probably better tolerated**

HCQ + Azithro – “Open label” non-RCT

ELSEVIER

International Journal of Antimicrobial Agents

Available online 20 March 2020, 105949

In Press, Journal Pre-proof

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret [a, b, $], Jean-Christophe Lagier [a, c, $], Philippe Parola [a, b], Van Thuan Hoang [a, b, d], Line Meddeb [a], Morgane Mailhe [a], Barbara Doudier [a], Johan Courjon [e, f, g], Valérie Giordanengo [h], Vera Esteves Vieira [a], Hervé Tissot Dupont [a, c], Stéphane Honoré [i, j], Philippe Colson [a, c], Eric Chabrière [a, c], Bernard La Scola [a, c], Jean-Marc Rolain [a, c], Philippe Brouqui [a, c], Didier Raoult [a, c]

Show more

https://doi.org/10.1016/j.ijantimicag.2020.105949

Get rights and content

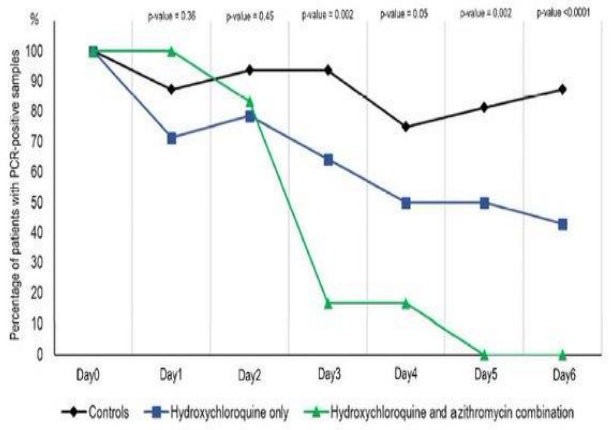
Abstract

- **Comparison of HCQ + Azithro vs. HCQ along vs. Control**
- **TWENTY patients showed significant reduction in viral carriage at day 6.**

Gautret et al. Int J of Antimicrobial Agents; March 20, 2020. https://doi.org/10.1016/j.ijantimicag.2020.105949

Results

Figure 2. Percentage of patients with PCR-positive nasopharyngeal samples from inclusion to day6 post-inclusion in COVID-19 patients treated with hydroxychloroquine only; in COVID-19 patients treated with hydroxychloroquine and azithomycin combination, and in COVID-19 control patients.



- **Viral "Eradication" Rates at Day 6:**
  - **HCQ + Azithro – 6/6 (100%)**
  - **HCQ along – 8/14 (57%)**
  - **Control – 2/16 (13%)**

- **Study started with 26 patients in HCQ and 16 controls**
  - **Six patients not evaluable at day 6**
    - **3 transferred to ICU while still PCR positive**
    - **1 died (PCR negative)**
    - **1 left the hospital (PCR negative)**
    - **1 withdrew due to nausea (PCR positive)**

Gautret et al. Int J of Antimicrobial Agents; March 20, 2020. https://doi.org/10.1016/j.ijantimicag.2020.105949
Jason Pogue's Twitter Account: https://twitter.com/jpogue1/status/1241138975802359813

Statement from ISAC

Statement on IJAA paper

Official Statement from International Society of Antimicrobial Chemotherapy (ISAC)

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial (Gautret P et al. PMID 32205204)

ISAC shares the concerns regarding the above article published recently in the International Journal of Antimicrobial Agents (IJAA). The ISAC Board believes the article does not meet the Society's expected standard, especially relating to the lack of better explanations of the inclusion criteria and the triage of patients to ensure patient safety.

Despite some suggestions online as to the reliability of the article's peer review process, the process did adhere to the industry's peer review rules. Given his role as Editor in Chief of this journal, Jean-Marc Rolain had no involvement in the peer review of the manuscript and has no access to information regarding its peer review. Full responsibility for the manuscript's peer review process was delegated to an Associate Editor.

Although ISAC recognises it is important to help the scientific community by publishing new data fast, this cannot be at the cost of reducing scientific scrutiny and best practices. Both Editors in Chief of our journals (IJAA and Journal of Global Antimicrobial Resistance) are in full agreement.

Andreas Voss
ISAC President

https://www.isac.world/news-and-publications/official-isac-statement

HCQ – Randomized Controlled Trial

34 comments

Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial

Zhaowei Chen, Jijia Hu, Zongwei Zhang, Shan Jiang, Shoumeng Han, Dandan Yan, Ruhong Zhuang, Ben Hu, Zhan Zhang

doi: https://doi.org/10.1101/2020.03.22.20040758

This article is a preprint and has not been certified by peer review [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Abstract | Info/History | Metrics | Preview PDF

- **62 patients randomized to either HCQ 400mg/day x5d + SOC vs. SOC alone**
- **Endpoints at day 5**
  - **Time to clinical recovery**
  - **Clinical characteristics**
  - **Radiological results**
- **Shorter time to clinical resolution of symptoms**
- **Not Peer Reviewed**

doi: https://doi.org/10.1101/2020.03.22.20040758

Results

Characteristics	All	Control	HCQ	P value
Cases, n	62	31	31	
Age, mean (SD)	44.7 (15.3)	45.2 (14.7)	44.1 (16.1)	0.8809
Sex, n (%)				0.7991
Male	29 (46.8%)	15 (48.3%)	14 (45.2%)	
Female	33 (53.2%)	16 (51.7%)	17 (54.9%)	
Fever, day (SD)[a]	2.6 (1.0)	3.2 (1.3)	2.2 (0.4)	0.0008
Cough, day (SD)[b]	2.4 (1.1)	3.1 (1.5)	2.0 (0.2)	0.0016
Progressed to severe illness	4 (6.5 %)	4 (12.9 %)	0	
Adverse effects	2 (3.2 %)	0	2 (6.4 %)	

Table 1: Characteristics of patients in this trial.

[a]22 patients in the HCQ treatment group,17 patients in the control group with a fever one day before the intervention. [b]22 patients in the HCQ treatment group,15 patients in the control group with a cough one day before the intervention. Abbreviations: SD, standard deviation; HCQ, hydroxychloroquine; CT, computed tomography.

Group	All	Exacerbated	Unchanged	Improved		
				Moderate	Significant	Total
All	62	11 (17.7 %)	9 (14.5 %)	18 (29.0 %)	24 (38.7 %)	42 (67.7 %)
Control, n (%)	31	9 (29.0 %)	5 (16.1%)	12 (38.7 %)	5 (16.1%)	17 (54.8%)
HCQ, n (%)	31	2 (6.5 %)	4 (12.9 %)	6 (19.4%)	19 (61.3%)	25 (80.6%)
P value	0.0476					

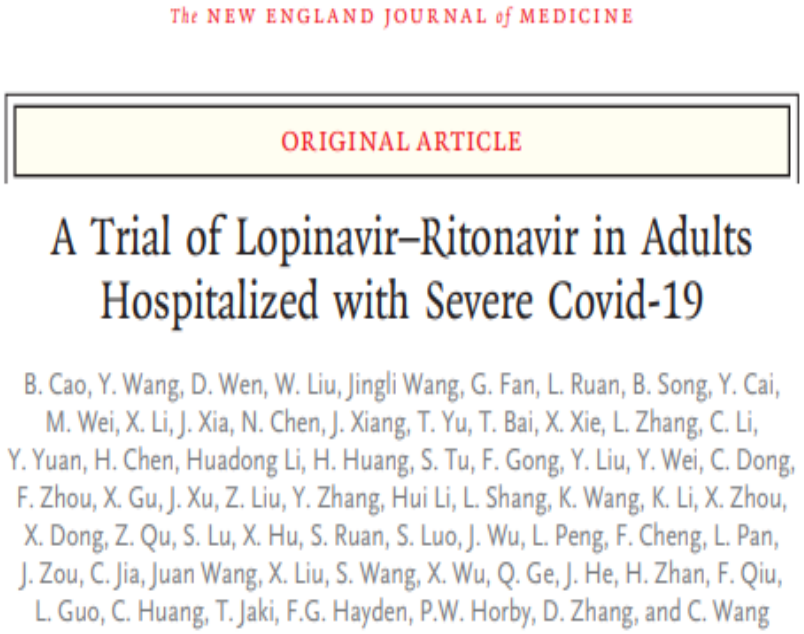
Table 2: Absorption of pneumonia on chest CT.

Abbreviations: HCQ, hydroxychloroquine.

doi: https://doi.org/10.1101/2020.03.22.20040758

Lopinavir/Ritonavir

- **Lopinavir is a protease inhibitor that blocks viral replication by inhibiting viral proteinase (vital role in protein processing and virus maturation)**
- **Ritonavir “boosts” lopinavir concentration**
- **May be effective when used in combination with other drugs**
- **Beware DDI**



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

B. Cao, Y. Wang, D. Wen, W. Liu, Jingli Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, X. Li, J. Xia, N. Chen, J. Xiang, T. Yu, T. Bai, X. Xie, L. Zhang, C. Li, Y. Yuan, H. Chen, Huadong Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, Hui Li, L. Shang, K. Wang, K. Li, X. Zhou, X. Dong, Z. Qu, S. Lu, X. Hu, S. Ruan, S. Luo, J. Wu, L. Peng, F. Cheng, L. Pan, J. Zou, C. Jia, Juan Wang, X. Liu, S. Wang, X. Wu, Q. Ge, J. He, H. Zhan, F. Qiu, L. Guo, C. Huang, T. Jaki, F.G. Hayden, P.W. Horby, D. Zhang, and C. Wang

- **RCT in 199 hospitalized adult patients with confirmed COVID-19.**
- **400/100mg BID x14 days plus SOC vs. SOC alone**
- **Mortality and detectable viral RNA were similar in both groups**
- **More GI ADR in tx group**

Wang et al. NEJM; March 18, 2020.
DOI: 10.1056/NEJMoa2001282

Remdesivir

- Available for investigational use only
- Adenosine-analog antiviral that inhibits RNA synthesis
- Activity against MERS-CoV, SARS, Ebola
- Study dose in adults: RDV 200 mg loading dose on day 1 is given, followed by 100 mg iv once-daily maintenance doses for 9 days
- Data is slowly becoming available
  - SIMPLE Trial data expected end of May 2020
- May 1, 2020 granted FDA Emergency Use Authorization
- Can be acquired from Gilead for compassionate use
  - Email to contact Gilead: coronavirus.response@gilead.com
  - AmerisourceBergen Remdesivir line: 1-877-987-4987

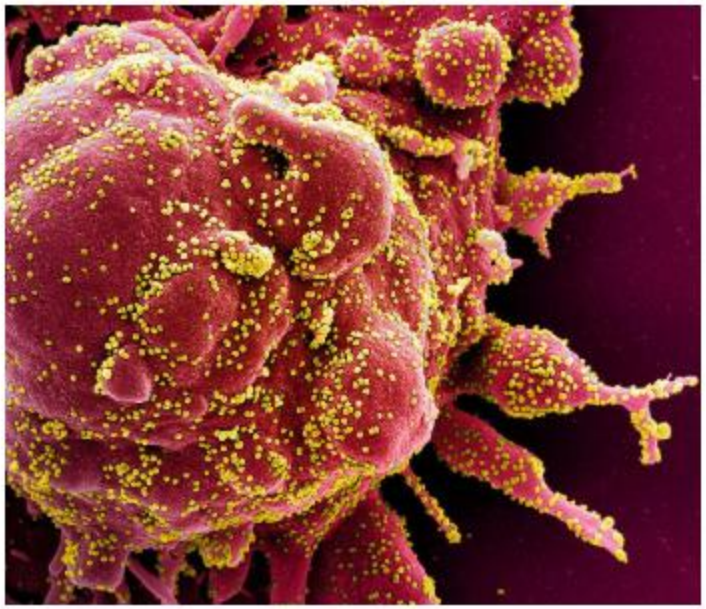
https://www.gilead.com/news-and-press/press-room/press-releases/2020/4/gilead-announces-results-from-phase-3-trial-of-investigational-antiviral-remdesivir-in-patients-with-severe-covid-19

Wednesday, April 29, 2020

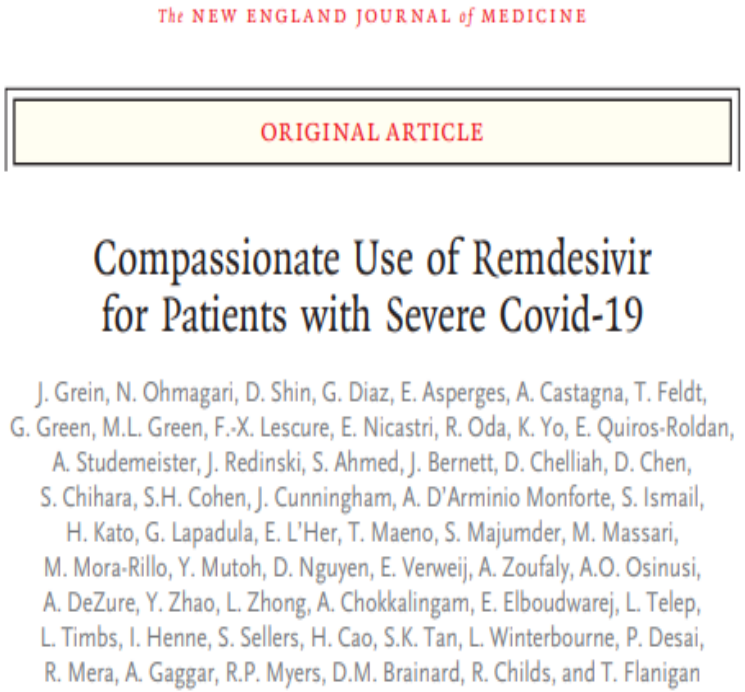
NIH clinical trial shows Remdesivir accelerates recovery from advanced COVID-19

Hospitalized patients with advanced COVID-19 and lung involvement who received remdesivir recovered faster than similar patients who received placebo, according to a preliminary data analysis from a randomized, controlled trial involving 1063 patients, which began on February 21. The trial (known as the Adaptive COVID-19 Treatment Trial, or ACTT), sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, is the first clinical trial launched in the United States to evaluate an experimental treatment for COVID-19.

An independent data and safety monitoring board (DSMB) overseeing the trial met on April 27 to review data and shared their interim analysis with the study team. Based upon their review of the data, they noted that remdesivir was better than placebo from the perspective of the primary endpoint, time



https://www.nih.gov/news-events/news-releases/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

J. Grein, N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M.L. Green, F.-X. Lescure, E. Nicastri, R. Oda, K. Yo, E. Quiros-Roldan, A. Studemeister, J. Redinski, S. Ahmed, J. Bernett, D. Chelliah, D. Chen, S. Chihara, S.H. Cohen, J. Cunningham, A. D'Arminio Monforte, S. Ismail, H. Kato, G. Lapadula, E. L'Her, T. Maeno, S. Majumder, M. Massari, M. Mora-Rillo, Y. Mutoh, D. Nguyen, E. Verweij, A. Zoufaly, A.O. Osinusi, A. DeZure, Y. Zhao, L. Zhong, A. Chokkalingam, E. Elboudwarej, L. Telep, L. Timbs, I. Henne, S. Sellers, H. Cao, S.K. Tan, L. Winterbourne, P. Desai, R. Mera, A. Gaggar, R.P. Myers, D.M. Brainard, R. Childs, and T. Flanigan

- **61 patients (53 analyzed)**
- **No control group**
- **Severe respiratory disease due to SARS-CoV-2**
- **36/53 (68%) showed clinical improvement in median followup of 18d.**
- **7 deaths**

Grein et al. NEJM; April 10, 2020.
DOI: 10.1056/NEJMoa2007016

Tocilizumab + Steroids

- **Interleukin-6 inhibitor**
- **May be helpful in cytokine storm associated with severe disease**
  - **After other therapies have failed?**

Evidence in Small Studies

- 20 severe or critical patients
- All received lopinavir, methylpred and supportive care plus toculizumab 400mg IV once
- Fever in all patients returned to normal by day following treatment
- 75% had improved oxygen intake
- Improvements in CRP and WBC in all but two patients.

- 15 patients (7 critically ill)
- Used in combination with methylpred in 8 patients
- 5 patients received more than once
- All patients had increases in CRP ameliorated
- Serum IL-6 spiked then declined in 10 patients
  - 4 patients who failed had dramatically increased IL-6

Luo et al. Journal of Medical Virology; April 6. 2020. https://doi.org/10.1002/jmv.25801, https://t.co/2LmKN34HjM?amp=1

Ways Pharmacists Can Help

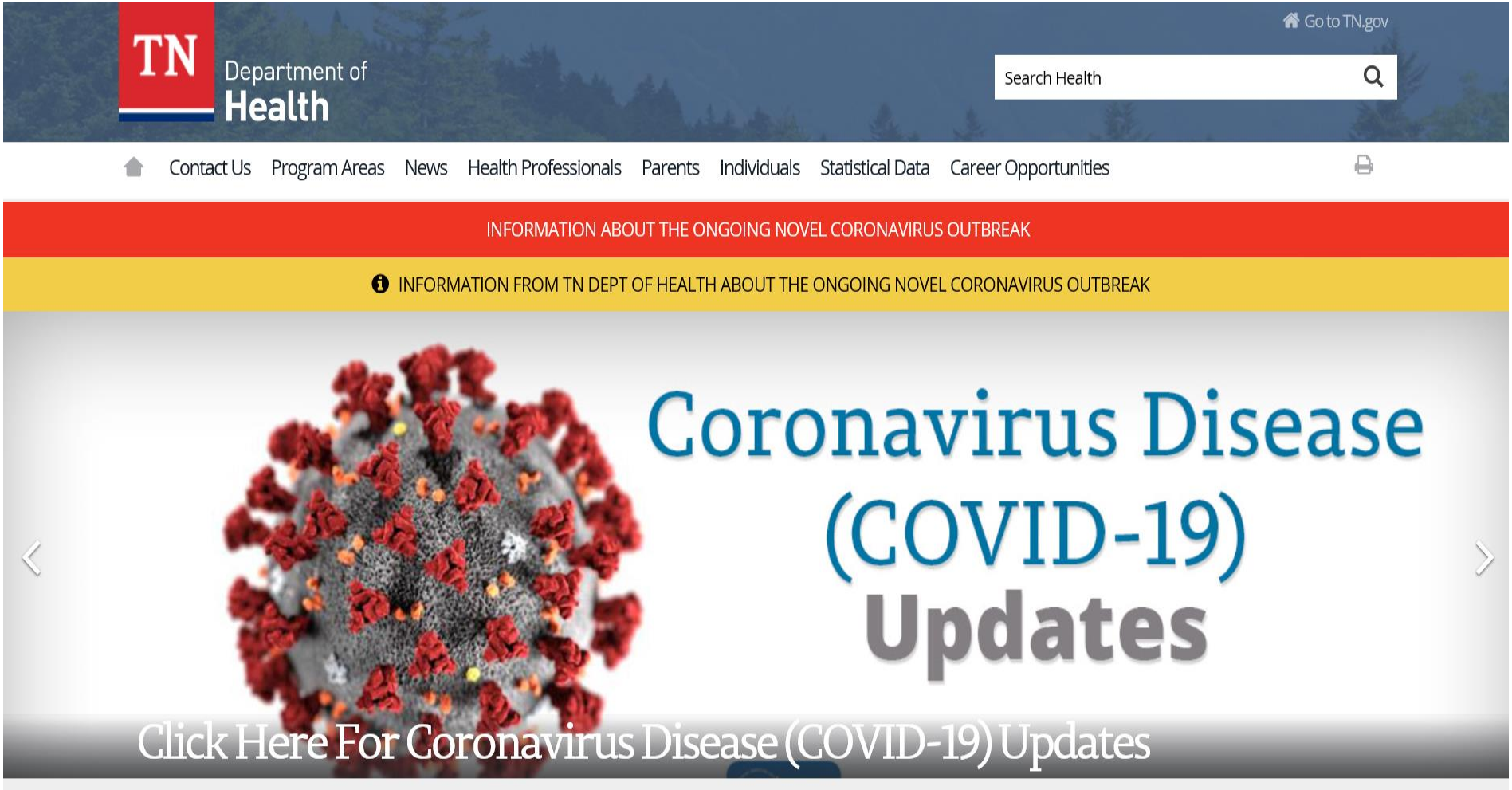
- **Be a role model and educate others about infection prevention basics**
- **Provide guidance to patients and customers**
- **Offer strategies for symptom management**
- **Direct people to reliable resources**
- **Keep up to date**

Resources

Good Treatment Resources

- Coronavirus Information for Pharmacists
  - https://www.idstewardship.com/coronavirus-covid-19-resources-pharmacists/
- IDSA Guidelines on Treatment and Management of Patients with COVID-19
  - https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/
- SIDP Review of Early and Emerging Options
  - https://academic.oup.com/ofid/article/7/4/ofaa105/5811022

https://TN.Gov/Health



https://TN.Gov/Health

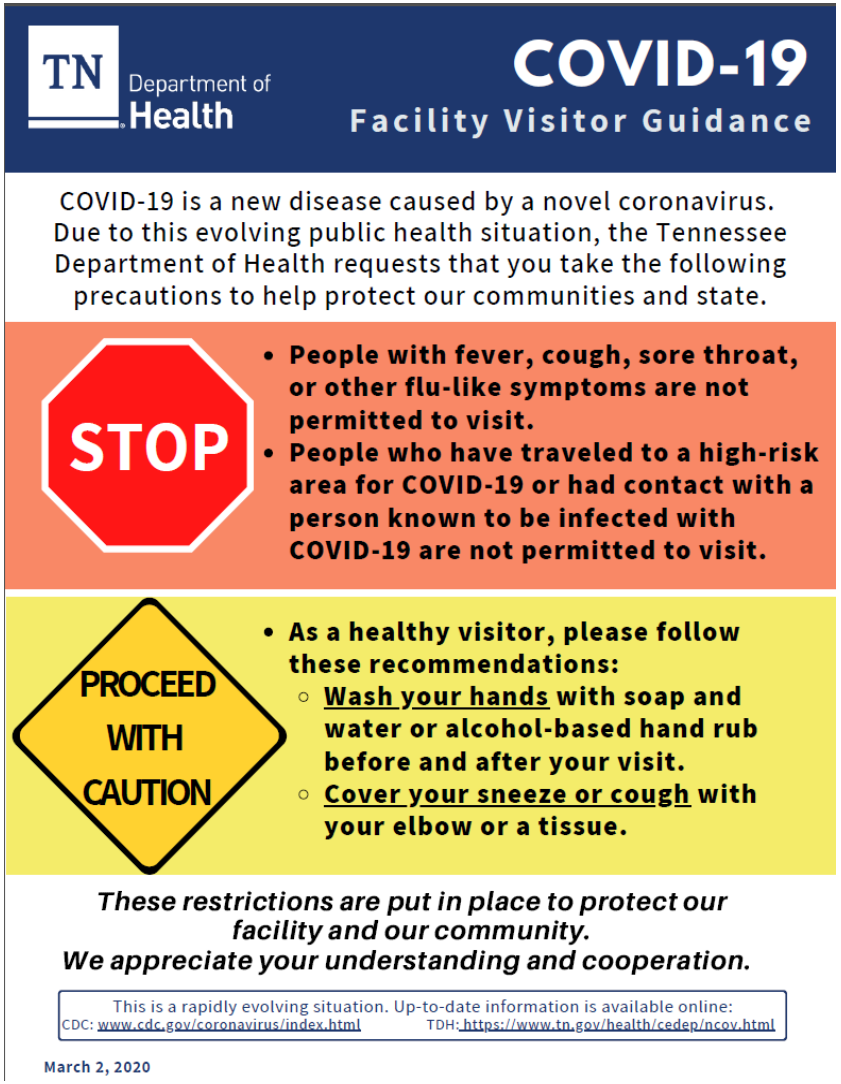
- For the Public
- Health Care Providers
- Laboratories
- Public Health
- Preparedness Tools
- Resources for Educational Organizations
- Resources for Congregate Care, Homeless, and Correctional Facilities

https://TN.Gov/Health

For the Public

- Learn more about this disease
- What to Expect After Being Diagnosed
  - What to Expect After Being Diagnosed (Spanish)
- What to Expect If You Were Possibly Exposed
  - What to Expect If You Were Possibly Exposed (Spanish)
- What to Expect After Being Tested
  - What to Expect After Being Tested (Spanish)
- CDC Guidance for Travelers
- Facility Visitor Guidance
- Interim Guidelines: Businesses & Employers
- Interim Guidelines: Mass Gatherings/Large Community Events
- Guidance for Faith-Based Organizations
  - Guidance for Faith-Based Organizations (Spanish)

Prevent introduction into facility



TN Department of Health

COVID-19
Facility Visitor Guidance

COVID-19 is a new disease caused by a novel coronavirus. Due to this evolving public health situation, the Tennessee Department of Health requests that you take the following precautions to help protect our communities and state.

STOP

- **People with fever, cough, sore throat, or other flu-like symptoms are not permitted to visit.**
- **People who have traveled to a high-risk area for COVID-19 or had contact with a person known to be infected with COVID-19 are not permitted to visit.**

PROCEED WITH CAUTION

- **As a healthy visitor, please follow these recommendations:**
  - **Wash your hands with soap and water or alcohol-based hand rub before and after your visit.**
  - **Cover your sneeze or cough with your elbow or a tissue.**

These restrictions are put in place to protect our facility and our community.
We appreciate your understanding and cooperation.

This is a rapidly evolving situation. Up-to-date information is available online:
CDC: www.cdc.gov/coronavirus/index.html TDH: https://www.tn.gov/health/cedep/ncov.html

March 2, 2020

https://TN.Gov/Health

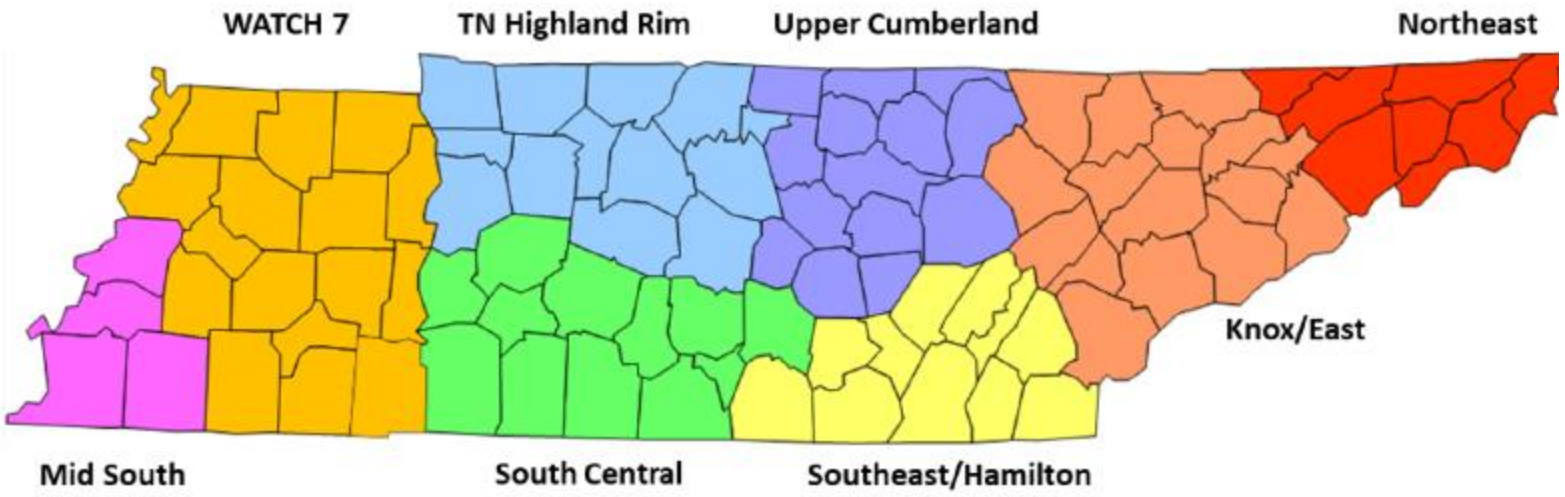
Health Care Providers

- TDH COVID-19 Webinars for Health Care Providers (held every Friday at noon!)
- Triage and assessment
- Clinical information about this disease
- Report a case of this disease
- Submit a specimen for laboratory testing
- Strategies for Optimizing the Supply of N95 Respirators
- PPE Conservation Guidance
- Application for Executive Order
- Guidance for Healthcare Workers Diagnosed with COVID
- Guidance for HealthCare Workers Returning to Work after COVID Illness
- Extended Use and Re-Use of N95s
- Extended Use and Re-Use of Facemasks
- Extended Use and Re-Use of Eye Protection

Additional resources

- **Infection preventionist training:**
  - **https://www.cdc.gov/longtermcare/index.html**
- **CDC Resources for Long-Term Facilities:**
  - https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/prevent-spread-in-long-term-care-facilities.html
- **CDC Preparedness Checklist for LTC:**
  - https://www.cdc.gov/coronavirus/2019-ncov/downloads/novel-coronavirus-2019-Nursing-Homes-Preparedness-Checklist_3_13.pdf
- **CDC COVID-19 Update and Information for LTCFs:**
  - **https://emergency.cdc.gov/coca/calls/2020/callinfo_031720.asp**
- **CDC FAQ for COVID-19:**
  - **https://www.cdc.gov/coronavirus/2019-ncov/infection-control/infection-prevention-control-faq.html**
- **Infection control toolkit for bedside licensed nurses and nurse aides:**
  - **https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/LTC-CMP-Reinvestment**
- **Infection control and Prevention regulations and guidance: 42 CFR 438.80, Appendix PP of the State Operations Manual. See F-tag 880:**
  - **https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/GuidanceforLawsAndRegulations/Downloads/Appendix-PP-State-Operations-Manual.pdf**

Regional Healthcare Coalition Contacts



Mid South Emergency Planning Coalition - http://www.midsouthepc.org/
Heather Fortner | 901-222-8216 | heather.fortner@shelbycountytn.gov

WATCH (West Area Healthcare Coalition)
Josh Moore | 731-421-5383 | josh.moore@tn.gov
Wayne Arnold | warnold@madisoncountytn.gov

TN Highland Rim Healthcare Coalition - https://tnhrhcc.com/
Tabitha Finney | 615-650-7009 | Tabitha.Finney@tn.gov
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South Central Region Healthcare Coalition - https://www.scrhccoalition.org/
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Southeast/Hamilton Regional Healthcare Coalition -
http://health.hamiltontn.org/EmergencyPreparedness/HealthcareCoalition.aspx
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Knox/East Tennessee Healthcare Coalition - http://www.ketcoalition.org/
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Wanda Roberts 865-549-5294 | Wanda.Roberts@tn.gov

Northeast/Sullivan Healthcare Coalition - https://nethealthcoalition.org/
Merenda Belcher | 423-279-2691 | mbelcher@sullivanhealth.org
Anthony Wright | 423-979-4633 | anthony.c.wright@tn.gov

Upper Cumberland Healthcare Preparedness Coalition – https://www.facebook.com/pg/UCCoalition/about/
Kristi Langford | 931-646-7547 | Kristi.langford@tn.gov

Announcements

Weekly Long-term Care Facility Updates

- **Occurs every Wednesday effective Wednesday, April 15, 2020 from 12:00 PM to 1:00 PM, (UTC-05:00) Central Time (US & Canada)**
- **12:00 pm | (UTC-05:00) Central Time (US & Canada) 1 hr**
- **Join meeting**
- **Join by phone**
- **Tap to call in from a mobile device (attendees only)**
- **+1-415-655-0003 US TOLL**
- **Meeting number (access code): 613 502 018**
- **Meeting password: MExYMZ5sP49**

Next Steps

- **Next Call**
  - **June 2, 2020 at 1 pm Eastern Time/ 12 pm Central time**

- **Opportunities for Involvement**
  - **Speaker or Topic for future call**
  - **NHSN Reporting**
  - **TDH Antibiotic Use Point Prevalence Survey**

- **Feedback always appreciated**
  - **HAI.Health@tn.gov**
  - **Cullen.Adre@tn.gov**
  - **Vicky.Reed@tn.gov**