The Daily COVID-19 Literature Surveillance Summary

September 11, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Climate

- Researchers collected self-reported data from a survey of 1,010 people across the United States and found that Americans have experienced an increase in conflict in romantic relationships, which was associated with changes in their engagement in intimate and sexual behaviors since the spread of COVID-19.

- An interdisciplinary group of physicians, public health specialists, and mass communication experts discuss the implicit meaning behind the question "when will we have a vaccine?" The authors assert that this question is not only one of time-frame, but also that of safety and effectiveness. They suggest that if a vaccine were to be ready for distribution, there needs to be easily accessible information available to the public for assurances that the vaccine not only works, but is also safe and effective.

Epidemiology

- Professors of economics, psychology, and psychiatry found that based on actuarial analysis of data from the Provisional COVID-19 Death Counts by Sex, Age, and State published by the CDC, the United States has garnered an estimated 1.2 million years of life lost due to COVID-19 from February 1 through July 11, 2020.

- An observational study of 164 locally transmitted COVID-19 cases admitted to a Singapore hospital found that the median incubation period was 5 days and that in general older age groups had longer incubation durations. The authors suggest that a longer incubation duration may reflect a delayed immune response and severe disease as seen in older patients, posing that the elderly population may benefit from earlier COVID-19 testing.

Transmission & Prevention

- A hospital-based retrospective study of 435 medical staff in Wuhan, China found that thymosin drugs did not provide adequate pre-exposure nor post-exposure SARS-CoV-2 prophylaxis. Although thymosin drugs were used as prophylaxis during previous SARS and MERS outbreaks, the authors do not recommend thymosin drugs as prophylaxis for COVID-19.

Management

- Investigators performed a systematic review and meta-analysis of 20 studies on COVID-19 and renin-angiotensin-aldosterone system (RAAS) inhibitors, including 28,872 patients with COVID-19. They found that ACEi/ARBS use for hypertensive patients exhibited a significant reduced association with death as well as for death and critical outcomes together. Although limited by high heterogeneity between studies, these findings suggest that patients currently on RAAS inhibitors should continue to use their medication during the COVID-19 pandemic.

R&D: Diagnosis & Treatments

- A study conducted across several medical institutions in Boston utilized a recently developed Single Molecular Assay (Simoa) to quantitatively detect SARS-CoV-2 antigens in serum. They detected S1 and N antigens in 41/64 COVID-19 patients with high S1 antigen concentration correlating with increased ICU admission rate (77%) and decreased time to intubation (<1 day). These findings suggest viral fragments can enter the bloodstream, possibly via tissue damage secondary to COVID-19 infection, thus making these quantitative values a potentially effective way to detect presence of SARS-CoV-2 and estimate disease severity.

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ROMANTIC RELATIONSHIP CONFLICT DUE TO THE COVID-19 PANDEMIC AND CHANGES IN INTIMATE AND SEXUAL BEHAVIORS IN A NATIONALLY REPRESENTATIVE SAMPLE OF AMERICAN ADULTS

Luetke M, Hensel D, Herbenick D, Rosenberg M.. J Sex Marital Ther. 2020 Sep 3:1-16. doi: 10.1080/0092623X.2020.1810185. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

Interdisciplinary researchers affiliated with Indiana University School of Public Health-Bloomington collected self-reported data from a survey distributed to adults (n=1,010 ; ≥18 years) across the United States from April 10 to April 20, 2020. Survey findings revealed that Americans have experienced an increase in conflict in romantic relationships, which was associated with changes in their engagement in intimate and sexual behaviors since the spread of COVID-19 (results are summarized below). The authors call to attention the importance of reducing the spillover effect of COVID-19-related stress into romantic relationships.

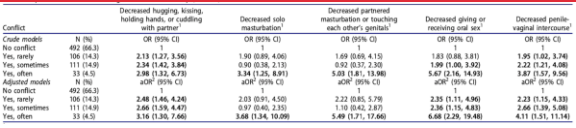
SUMMARY

• 34% of individuals in romantic relationships reported some degree of conflict related to the COVID-19 pandemic.
• Compared to individuals not experiencing any relationship conflicts, individuals experiencing frequent COVID-19-related conflict were more likely to report decreased frequency of several solo and partnered intimate and sexual behaviors (Table 2, Figure 1).
• COVID-19-related conflict was also related to decreased experience of orgasm and "feeling emotionally close to partner at last sexual event in the last month" among individuals in a relationship who engaged in sexual activity in the last month (Table 4).

ABSTRACT

In early 2020, the novel coronavirus 2019 (COVID-19) spread across the United States and mitigation measures drastically affected the daily lives of Americans. In this study, we assessed the association between COVID-related relationship conflict and changes in intimate and sexual behaviors and experiences. Using data from an online nationally representative probability survey of 1,010 American adults in April 2020, we estimated the impact of coronavirus-related relationship conflict on changes in intimate and sexual behaviors among those in any type of romantic or sexual relationship (Nweighted=742). Further, we assessed the association between conflict and experience of orgasm and feeling emotionally close to partner. Among individuals in relationships, 34% reported some degree of conflict with their romantic partners due to the spread of COVID-19 and its related restrictions. Those experiencing frequent coronavirus-related conflict with their partner were significantly more likely to report decreased frequency of several solo and partnered intimate and sexual behaviors compared to those not experiencing any such conflict, exhibiting a dose-response trend among partnered sexual behaviors. Since the spread of coronavirus and associated social distancing measures in the United States, Americans have experienced escalations in conflict in their romantic partnerships, which was associated with changes to their intimate and sexual lives.

FIGURES



Conflict		Decreased hugging, kissing, holding hands, or cuddling with partner[1]	Decreased solo masturbation[1]	Decreased partnered masturbation or touching each other's genitals[1]	Decreased giving or receiving oral sex[1]	Decreased penile-vaginal intercourse[1]
Crude models	N (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
No conflict	492 (66.3)	1	1	1	1	1
Yes, rarely	106 (14.3)	**2.13 (1.27, 3.56)**	1.90 (0.89, 4.06)	1.69 (0.69, 4.15)	1.83 (0.88, 3.81)	**1.95 (1.02, 3.74)**
Yes, sometimes	111 (14.9)	**2.34 (1.42, 3.84)**	0.90 (0.38, 2.13)	0.92 (0.37, 2.30)	**1.99 (1.00, 3.92)**	**2.22 (1.21, 4.08)**
Yes, often	33 (4.5)	**2.98 (1.32, 6.73)**	**3.34 (1.25, 8.91)**	**5.03 (1.81, 13.98)**	**5.67 (2.16, 14.93)**	**3.87 (1.57, 9.56)**
Adjusted models	N (%)	aOR[2] (95% CI)	aOR[2] (95% CI)	aOR[2] (95% CI)	aOR[2] (95% CI)	aOR[2] (95% CI)
No conflict	492 (66.3)	1	1	1	1	1
Yes, rarely	106 (14.3)	**2.48 (1.46, 4.24)**	2.03 (0.91, 4.50)	2.22 (0.85, 5.79)	**2.35 (1.11, 4.96)**	**2.23 (1.15, 4.33)**
Yes, sometimes	111 (14.9)	**2.66 (1.59, 4.47)**	0.97 (0.40, 2.35)	1.10 (0.42, 2.87)	**2.36 (1.15, 4.83)**	**2.66 (1.39, 5.08)**
Yes, often	33 (4.5)	**3.16 (1.30, 7.66)**	**3.68 (1.34, 10.09)**	**5.49 (1.71, 17.66)**	**6.68 (2.29, 19.48)**	**4.11 (1.51, 11.14)**

Table 2. Unadjusted and adjusted logistic regression for the associations between frequency of coronavirus-related relationship conflict and decreases in frequency of intimate behaviors since the spread of coronavirus among those in a relationship (N=742).

1All outcomes dichotomized as 1=Decrease (i.e. A little Less/Much Less) vs. 0=Stable or increase (No Change/ A Little More/Much More).
2Adjusted for children aged 12 or younger in household (yes/no), age (in years), and living with partner (yes/no).

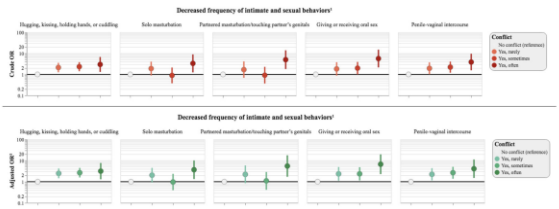


Figure 1. Forest plots of the unadjusted and adjusted logistic regression for the associations between frequency of coronavirus- related relationship conflict and decreases in frequency of intimate behaviors since the spread of coronavirus among those in a relationship (N 1/4 742)

1All outcomes dichotomized as 1=Decrease (i.e. A little Less/Much Less) vs. 0=Stable or increase (No Change/ A Little More/ Much More).
2Adjusted for children aged 12 or younger in household (yes/no), age (in years), and living with partner (yes/no).

Conflict		Experienced orgasm at last sex	Felt emotionally close to partner at last sex
Unadjusted models	N (%)	OR (95% CI)	OR (95% CI)
No conflict	275 (65.8)	1	1
Some conflict[1]	143 (34.2)	0.92 (0.57, 1.46)	0.86 (0.55, 1.35)
Adjusted models	N (%)	aOR[2] (95% CI)	aOR[2] (95% CI)
No conflict	275 (65.8)	1	1
Some conflict[1]	143 (34.2)	0.90 (0.56, 1.47)	0.85 (0.54, 1.34)

Table 4. Unadjusted and adjusted logistic regression for the associations between frequency of coronavirus-related relationship conflict and orgasm and feeling connected to partner at last sexual event, among those in a relationship and who had engaged in sexual activity in last month (N=418).

1Some conflict combined responses (1) yes, rarely, (2) yes, sometimes, and (3) yes, often.
2Adjusted for children aged 12 or younger in household (yes/no), age (in years), and living with partner (yes/no).

"WHEN WILL WE HAVE A VACCINE?" - UNDERSTANDING QUESTIONS AND ANSWERS ABOUT COVID-19 VACCINATION

Bloom BR, Nowak GJ, Orenstein W.. N Engl J Med. 2020 Sep 8. doi: 10.1056/NEJMp2025331. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

An interdisciplinary group of physicians, public health specialists, and mass communication authors from Boston, Atlanta, and Athens penned an opinion piece on the implicit meaning behind the question "when will there be a COVID-19 vaccine ready?" The authors assert that this question is not only one of time-frame, but also that of safety and effectiveness. They suggest that if a vaccine were to be ready for distribution, there needs to be easily accessible information available to the public for assurances that the vaccine not only works, but is also safe and effective.

SUMMARY

In this opinion piece, the authors attempt to elucidate the meaning behind the question of when a vaccine for COVID-19 will be available. The authors assert that this question is actually multifaceted in that not only does the public want to know when the vaccine will be ready but also within the question lies subtext related vaccination issues beyond time-frames. The authors believe that the question of "when will we have a vaccine?" actually means:

- When will the vaccine be available?
- Will the vaccine be safe?
- Will the uptake of the vaccine be enough to return to prepandemic levels?

The authors further expound on the ideas of what is needed to properly roll out a new vaccine and for it to be successful. They believe that due to recent politicization of the pandemic there needs to be a commitment from the FDA and drug manufacturers to having information that is easily understood and readily available to the public about the safety and effectiveness of the impending vaccine. They further explain that certain criteria such as prioritized groups need to be established in order to ensure that proper distribution of the vaccines are met.

The authors further assert that the public not rely on the idea that prioritized groups will take up the vaccines as assumed and that attempting to persuade ant-vaccination groups to vaccinate is difficult and often not successful. So even if a vaccine is developed, the number of estimated individuals wanting the vaccine may be lower than expected.

Finally, the authors state that healthcare workers are highly trusted professionals in the public eye and that if a vaccine were to be successful, it would depend on the endorsement of doctors, nurses, pharmacists worldwide.

YEARS OF LIFE LOST ASSOCIATED WITH COVID-19 DEATHS IN THE UNITED STATES

Quast T, Andel R, Gregory S, Storch EA.. J Public Health (Oxf). 2020 Sep 7:fdaa159. doi: 10.1093/pubmed/fdaa159. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

Professors of economics, psychology, and psychiatry found that based on actuarial analysis of data from the Provisional COVID-19 Death Counts by Sex, Age, and State published by the CDC, the United States garnered an estimated 1.2 million years of life lost (YLL) due to COVID-19 from February 1 through July 11, 2020. This is a new statistic reflecting the immense impact of the pandemic on our population (Figures 1-2).

ABSTRACT

BACKGROUND: The mortality effects of COVID-19 are a critical aspect of the disease's impact. Years of life lost (YLLs) can provide greater insight than the number of deaths by conveying the shortfall in life expectancy and thus the age profile of the decedents. METHODS: We employed data regarding COVID-19 deaths in the USA by jurisdiction, gender and age group for the period 1 February 2020 through 11 July 2020. We used actuarial life expectancy tables by gender and age to estimate YLLs. RESULTS: We estimated roughly 1.2 million YLLs due to COVID-19 deaths. The YLLs for the top six jurisdictions exceeded those for the remaining 43. On a per-capita basis, female YLLs were generally higher than male YLLs throughout the country. CONCLUSIONS: Our estimates offer new insight into the effects of COVID-19. Our findings of heterogenous rates of YLLs by geography and gender highlight variation in the magnitude of the pandemic's effects that may inform effective policy responses.

FIGURES

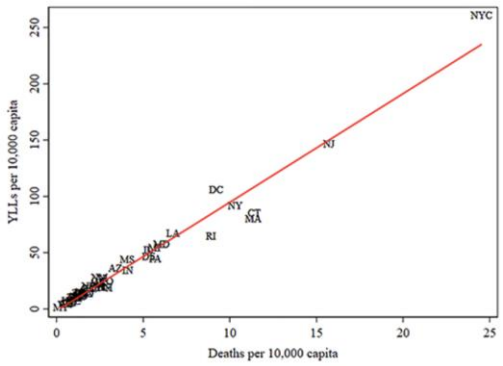


Fig 1. Years of life lost (YLLs) and deaths per 10,000 capita.

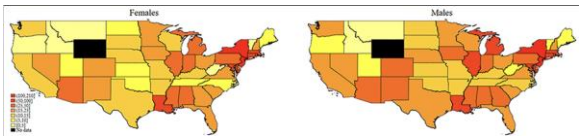


Fig 2. YLLs per 10,000 capita by gender.

DOES INCUBATION PERIOD OF COVID-19 VARY WITH AGE? A STUDY OF EPIDEMIOLOGICALLY LINKED CASES IN SINGAPORE

Tan WYT, Wong LY, Leo YS, Toh MPHS.. Epidemiol Infect. 2020 Sep 2:1-16. doi: 10.1017/S0950268820001995. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

In this retrospective observational study (n=164), researchers from multiple healthcare institutions in Singapore actively mapped epidemiological data from locally transmitted COVID-19 cases admitted to the hospital between January 23 to April 2, 2020. They found that the median incubation period was 5 days (range: 1 to 12 days; Figure 1), and that older age groups, except those between ages of 60 to 69, had longer incubation durations (Table 2). Additionally, mean incubation duration of patients less than 70 years was less than patients 70 years and older (5.43 vs 7.56 days, p = 0.008; Figure 2). The authors suggest that a longer incubation duration may reflect a delayed immune response and severe disease as seen in older patients, posing that the elderly population may benefit from earlier COVID-19 testing.

FIGURES

Age group (years)	No. ($n = 159$)[a]	Length of hospital stay (days)	
		Mean ± S.D.	Median (range)
Total	**115**	**14.6 ± 8.1**	**13.0 (3–64)**
Below 30	16	13.6 ± 5.6	13.5 (6–22)
30–39	27	11.8 ± 4.7	13.0 (3–25)
40–49	23	13.0 ± 4.4	14.0 (5–20)
50–59	24	15.7 ± 6.4	14.5 (6–31)
60–69	18	18.7 ± 15.2	13.0 (6–64)
70 and above	7	17.7 ± 9.4	15.0 (9–38)

S.D., standard deviation.
[a]Excluded two cases that were still admitted and three death cases. Missing values: 44 cases (27.7%).

Table 2. Breakdown of length of stay according to age groups

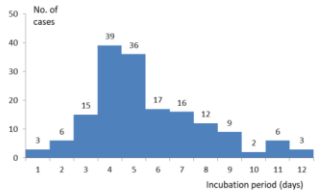


Figure 1. Incubation period of patients with known exposure to another positive case.

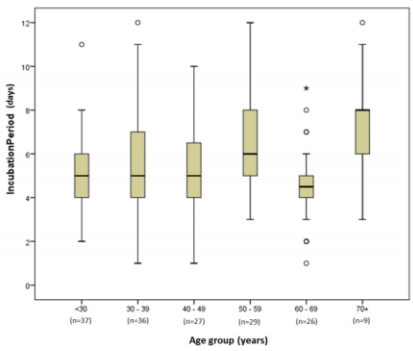


Figure 2. Box plot of incubation period byage group

DEVELOPMENTS IN TRANSMISSION & PREVENTION

ANALYSIS OF THE PROPHYLACTIC EFFECT OF THYMOSIN DRUGS ON COVID-19 FOR 435 MEDICAL STAFF: A HOSPITAL-BASED RETROSPECTIVE STUDY

Liu X, Liu Y, Wang L, Hu L, Liu D, Li J.. J Med Virol. 2020 Sep 8. doi: 10.1002/jmv.26492. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A hospital-based retrospective study of 435 medical staff at Tongji Hospital in Wuhan, China from January 25 to March 25, 2020 revealed through a questionnaire survey and examination of real-world data, that thymosin drugs did not provide adequate pre-exposure nor post-exposure SARS-CoV-2 prophylaxis. Although thymosin drugs were used as prophylaxis during previous SARS and MERS outbreaks, the authors could not recommend thymosin drugs as prophylaxis for COVID-19.

ABSTRACT

BACKGROUND: To explore the role of thymosin drugs in the prevention of a novel coronavirus disease (COVID-19), we analyzed the preventive effects of different medication timings on health medical staff, and then provided recommendations for pharmaceutical monitoring of the thymus drugs. METHODS: We conducted a hospital-based retrospective study on 435 medical staff who might use or not to use thymosin drugs for preventive medicines in our hospital. For the prophylactics, medical staff was prevented from pre-exposure prophylaxis (risk prevention of exposure to COVID-19 patients before using thymosin drugs) and post-exposure prophylaxis (risk prevention of exposure to COVID-19 patients with after using thymosin drugs). Effectiveness and safety of thymosin drugs in the prevention and control of COVID-19 application, in real world data research for the application of the drug in COVID- 19. RESULTS: In the similar exposure environment, compared to medical staff who did not take preventive medicine, the use of thymosin drugs, before exposure and after exposure had an insignificant effect, and the adverse drug reaction (ADR) was increased, especially when thymosin drugs used together with alpha-interferon. CONCLUSIONS: Thymosin drugs had no significant effect on the prevention of COVID-19 before and after exposure for medical staff, along with certain ADRs, so preventive medication of thymosin drugs was not recommended. This article is protected by copyright. All rights reserved.

RECONSIDERING ASSUMPTIONS OF ADOLESCENT AND YOUNG ADULT SARS-COV-2 TRANSMISSION DYNAMICS

Guilamo-Ramos V, Benzekri A, Thimm-Kaiser M, Hidalgo A, Perlman DC.. Clin Infect Dis. 2020 Sep 7:ciaa1348. doi: 10.1093/cid/ciaa1348. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Researchers affiliated with New York University and Icahn School of Medicine at Mount Sinai review evidence (summarized below) supporting a heightened potential for adolescents and young adults (AYA) to spread COVID-19. Based on this evidence, the authors believe that the AYA population need specific considerations in COVID-19 prevention and containment efforts. Further, the authors provide "programmatic suggestions" to assist future COVID-19 prevention and control specific to AYA population (Table 1).

SUMMARY

- The authors highlight emerging evidence that the median serial interval (the time between symptom onset for an index case and the date of symptom onset for secondary cases) for AYA may be significantly shorter (1–2 days) compared to in the general population (4–6 days). The authors argue that such evidence suggests that AYA is more prone to presymptomatic transmission compared to the older age cohort.
- The authors relate growing evidence for AYA being more likely to experience no or only mild symptoms compared to older age cohorts. The authors also point to a systematic review and meta-analysis which suggests that viral loads of symptomatic and asymptomatic individuals infected with SARS-CoV-2 are comparable. Thus, the authors argue that there is a potential increase in the risk of COVID-19 transmission by AYA infected with SARS-CoV-2 with no, mild, or atypical symptoms because current policies and guidelines prioritize severely symptomatic cases for COVID-19 testing.

ABSTRACT

Evidence regarding the important role of adolescents and young adults (AYA) in accelerating and sustaining coronavirus disease 2019 (COVID-19) outbreaks is growing. Furthermore, data suggest two known factors that contribute to high severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmissibility-presymptomatic transmission and asymptomatic case presentations-may be amplified in AYA. However, AYA have not been prioritized as a key population in the public health response to the COVID-19 pandemic. Policy decisions that limit public health attention on AYA and are driven by the assumption of insignificant forward transmission from AYA pose a risk to inadvertently reinvigorate local transmission dynamics. In this viewpoint, we highlight evidence regarding the increased potential of AYA to transmit SARS-CoV-2 that, to date, has received little attention, discuss adolescent and young adult specific considerations for future COVID-19 control measures, and provide applied programmatic suggestions.

FIGURES

Theme	Adolescent and Young Adult-Specific Consideration	Programmatic Suggestion
Adolescence and Young Adulthood as a Distinct Developmental Period	While evidence shows adolescents and young adults (AYA) acquire and transmit SARS-CoV-2, AYA have not been prioritized as a key population in the COVID-19 response.	Consideration of factors unique to AYA in the design, communication, and implementation of COVID-19 control measures is warranted.
	Adolescence and young adulthood is a distinct period of neurobiological development in which changing connectivity between brain regions results in the prioritization of short-term social and emotional reward (e.g., group interactions, normative life events), rather than the long- term health consequences of potential COVID-19 infection [S1][a].	Public health programs and messaging can emphasize the short-term socioemotional benefits of adopting COVID-19 measures for AYA (e.g.: face masks as a style accessory, social distancing as an opportunity to spend time with one's family, etc.) and the collective nature of the COVID-19 response (e.g., —We— AYA, peers, parents, other important influencers in AYA's lives—are all in this together!).
	COVID-19 related research is primarily focused on adults and vulnerable populations, with limited attention placed on early, middle, late adolescence and young adulthood.	Surveillance and research studies that disaggregate data by age, as well as focus on adolescent and young adult social, immune, endocrine, epigenetic, and clinical factors which may sustain COVID-19 outbreaks are needed.
Public Health Messaging	Incomplete uptake of COVID-19 protective behaviors among AYA has been depicted as irresponsible in the media and in public health messaging.	Punitive messaging is counterproductive and does not adequately recognize the conflict of normative AYA identity development and social distancing measures.
	Primary caregivers (i.e., parents) are an important influence on adolescent and young adult health behavior [S2, S3].	An emphasis on specific guidance for primary caregivers regarding COVID-19 communication and monitoring can address gaps in extant public health communication designed to shape AYA behavior.
	Public health messaging for AYA is primarily generic and has not provided specific guidance on how AYA can prevent transmission in their day-to-day lives.	Provide specific guidance regarding adolescent and young adult self-monitoring of symptoms, household behaviors (i.e., shared bathroom use), etc.
Preventing School/ University Transmission	The contribution of regular, in-person school/university education to accelerating and sustaining population-level outbreaks of COVID-19 is insufficiently understood.	Clear, evidence-based, and stakeholder-informed prevalence thresholds and plans for stepwise openings and closures should be developed and communicated by schools and universities [S4].
	Evidence-based best practices for a safe return to in-person instruction are needed.	Evaluation and optimization of recommended mitigation measures in schools/universities is needed (i.e., situate students at least 6 feet apart, reduce class sizes, minimize mixing between student class groups, assign permanent seating, use of outdoor spaces for classroom- related activities) [S5, S6].
	Mobility patterns such as cross-country travel of out-of-state university students may reinvigorate SARS-CoV-2 transmission in communities with controlled local epidemics.	Robust quarantine strategies for traveling students represent an essential piece of university COVID-19 mitigation plans. Attendance of in-state universities may reduce travel-related spread of COVID-19.

Table 1 (Part 1). Adolescent and Young Adult Programmatic Suggestions for Coronavirus Disease 2019 (COVID-19) Prevention and Control.

Notes: Subscript "a"-Table references are provided as Supplemental Material

COVID-19 Testing	Adolescence and young adulthood is a period of optimal health, in which AYA infected with SARS-CoV-2 may be more likely to experience mild, no, or atypical symptoms- making timely identification and isolation of AYA with COVID-19 a challenge.	High-volume, high-frequency, and symptom-unspecific testing in at-risk AYA populations (e.g. schools, universities) can reduce reproductive rates and account for the asymptomatic transmission potential among AYA [S7, S8].
	Frequent and widespread testing of asymptomatic AYA, for example in school or university settings, may be cost- prohibitive and takes up laboratory capacity.	Batch testing is scalable, cost-effective, and should be considered for school/university testing initiatives [S9, S10].
	School and university testing may exclude vulnerable AYA who are often disconnected from educational institutions (e.g. criminal justice-involved youth, pregnant or parenting youth, sexual/gender minority youth, youth with mental health issues).	Once available, point-of-care COVID-19 testing should be offered routinely in youth- serving health and social service organizations, particularly in vulnerable communities most heavily affected by COVID-19 [S11, S12].
Preventing Family/ Household Transmission	AYA are more likely than older individuals to co-reside with others (e.g., family members, roommates), increasing the risk of household transmission [S13].	Evidence-based and specific guidance to minimize transmission within households and among families, and particularly from AYA to parents and other family members, is needed.
	There is limited guidance that addresses the needs of AYA residing in households within low socioeconomic status communities.	Community-involved initiatives to develop culturally appropriate, feasible, effective, and replicable COVID-19 mitigation strategies within socially and economically vulnerable households is warranted [S14–S16].
Vaccines and Novel Prevention and Treatment Methods	AYA are a key population for efforts to promote uptake of COVID-19 prevention methods that are currently under development, including vaccines, particularly given that vaccination rates among AYA remain low and have decreased during the COVID-19 pandemic [S17, S18].	AYA participation in ongoing and future COVID-19 trials for vaccines, hyperimmune globulin and convalescent plasma therapy, pre-exposure and post-exposure prophylaxis is important. Behavioral interventions to promote the uptake of a novel COVID-19 vaccine as well as available influenza vaccines need to account for the unique needs of AYA.
	The implications of SARS-CoV-2 infection for vulnerable AYA populations is insufficiently understood.	Vulnerable adolescent and young adult populations warranting special attention in the development and evaluation of COVID-19 vaccines and novel prevention and treatment modalities include ethnic/racial minority AYA, pregnant youth, young substance users, and immunocompromised youth [S11, S19].

Continuation of Table 1 (Part 2). Adolescent and Young Adult Programmatic Suggestions for Coronavirus Disease 2019 (COVID-19) Prevention and Control.

Notes: Subscript "a"-Table references are provided as Supplemental Material

Long-Term Developmental and Socioeconomic Consequences	Social distancing recommendations are in conflict with normative AYA social development, contributing to increasing mental health problems among AYA.	To optimize adolescent and young adult social interactions, parents can be encouraged to spend additional time with their adolescent or young adult. Additionally, the seamless continuation of AYA behavioral health service delivery, remote or in person, is essential [S21, S21].
	COVID-19 control measures have disrupted AYA educational trajectories, thereby impacting long-term life trajectories and reducing life opportunities, particularly for socially vulnerable AYA.	Practical strategies to avoid adolescent disengagement in remote schooling, address technology/language barriers to online schooling, and ensure adequate learning environments at home are warranted.
	In the current recessionary economic climate, opportunities for AYA to enter the workforce are limited.	In the contemplated rollout of workforce-intensive COVID-19 mitigation initiatives such as contact tracing, community-based testing, or public health messaging, AYA training and professional development programs for key positions such as community health workers, contact tracers, etc. should be considered.
	COVID-19 prevention represents only one of many AYA health priorities shaping long-term adult health and wellbeing (e.g. sexual and reproductive health, mental health, etc.)	Universal access to youth-friendly COVID-19, primary and specialty healthcare, and auxiliary services is imperative for reducing long standing health disparities in the US. Existing non-COVID-19 specialty services for AYA represent an opportunity for integration of COVID-19 mitigation strategies.

Continuation of Table 1 (Part 3). Adolescent and Young Adult Programmatic Suggestions for Coronavirus Disease 2019 (COVID-19) Prevention and Control.

Notes: Subscript "a"-Table references are provided as Supplemental Material.

EFFECT OF RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM INHIBITORS IN PATIENTS WITH COVID-19: A SYSTEMATIC REVIEW AND META-ANALYSIS OF 28,872 PATIENTS

Baral R, White M, Vassiliou VS.. Curr Atheroscler Rep. 2020 Aug 24;22(10):61. doi: 10.1007/s11883-020-00880-6.
Level of Evidence: 2 - Systematic review of randomized trials or n-of-1 trial

BLUF

Investigators affiliated with Norfolk and Norwich University Hospital and Norwich Medical School performed a systemic review and meta-analysis of 20 studies on COVID-19 and renin-angiotensin-alosterone system (RAAS) inhibitors, including 28,872 patients with COVID-19 between inception and May 17, 2020. They found that patients on ACEi/ARBs exhibited a trend toward lower odds of death and critical events, although this trend was not significant (OR: 0.671, CI: 0.435 - 1.034, p = 0.071; Figure 1). Additionally, ACEi/ARBS use for hypertensive patients did exhibit a significant reduced association with deaths (OR: 0.664, CI: 0.458 to 0.964, p = 0.031; Figure 2) as well as for death and critical outcomes together (OR: 0.670, CI: 0.495 - 0.908, p = 0.010; Figure 1). Although limited by the large heterogeneity between studies, these findings suggest that patients currently on RAAS inhibitors should continue to use their medication during the COVID-19 pandemic.

ABSTRACT

PURPOSE OF REVIEW: The role of renin-angiotensin-aldosterone system (RAAS) inhibitors, notably angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs), in the COVID-19 pandemic has not been fully evaluated. With an increasing number of COVID-19 cases worldwide, it is imperative to better understand the impact of RAAS inhibitors in hypertensive COVID patients. PubMed, Embase and the pre-print database Medrxiv were searched, and studies with data on patients on ACEi/ARB with COVID-19 were included. Random effects models were used to estimate the pooled mean difference with 95% confidence interval using Open Meta[Analyst] software. RECENT FINDINGS: A total of 28,872 patients were included in this meta-analysis. The use of any RAAS inhibition for any conditions showed a trend to lower risk of death/critical events (OR 0.671, CI 0.435 to 1.034, p = 0.071). Within the hypertensive cohort, however, there was a significant lower association with deaths (OR 0.664, CI 0.458 to 0.964, p = 0.031) or the combination of death/critical outcomes (OR 0.670, CI 0.495 to 0.908, p = 0.010). There was no significant association of critical/death outcomes within ACEi vs non-ACEi (OR 1.008, CI 0.822 to 1.235, p = 0.941) and ARB vs non-ARB (OR 0.946, CI 0.735 to 1.218, p = 0.668). This is the largest meta-analysis including critical events and mortality data on patients prescribed ACEi/ARB and found evidence of beneficial effects of chronic ACEi/ARB use especially in hypertensive cohort with COVID-19. As such, we would strongly encourage patients to continue with RAAS inhibitor pharmacotherapy during the COVID-19 pandemic.

FIGURES

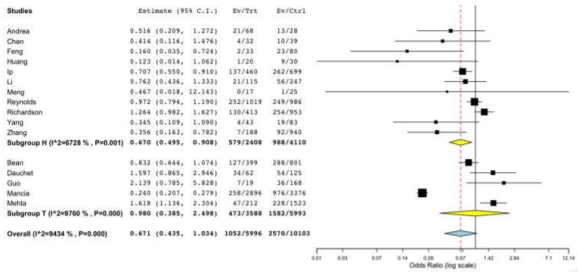


Fig. 1 Subgroup analysis of death/critical events in ACEi/ARB vs nonACEi/ARB. Subgroup analysis of death/critical events (OR 0.671, CI 0.435 to 1.034, p = 0.071) in sixteen studies with 5996 patients on ACEi/ARB vs 10,103 non-ACEi/ARB patients. Total effect for subgroup H with 11 studies (OR 0.670, CI 0.495 to 0.908, p = 0.010). Subgroups H and T refer to reference population; H is hypertension, T for sample population with mixed comorbidities. I^2 refers to I 2 as a measure of heterogeneity

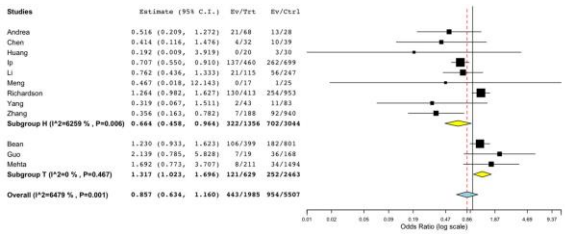


Fig. 2 Subgroup analysis of death in ACEi/ARB vs non-ACEi/ARB. Subgroup analysis of death in twelve studies (OR 0.857, CI 0.634 to 1.160, p = 0.318) in ACEi/ARB vs non-ACEi/ARB. Subgroup H with nine studies (OR 0.664, CI 0.458 to 0.964, p = 0.031). Subgroups H and T refer to reference population; H is hypertension; T for sample population with mixed comorbidities. I^2 refers to I2 as a measure of heterogeneity

ACUTE CARE

FATAL STROKE AS PRESENTATION OF SARS-COV-2 AND DENGUE VIRUS COINFECTION

Estofolete CF, Machado LF, Zini N, Luckemeyer GD, Moraes MM, Dos Santos TNIL, Dos Santos BF, Ruiz LGP, Vasilakis N, Lobo SMA, Nogueira ML.. J Med Virol. 2020 Sep 3. doi: 10.1002/jmv.26476. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Investigators affiliated with Faculdade de Medicina de São José do Rio Preto (FAMERP) and Hospital de Base in Brazil describe a 60 year-old obese, hypertensive female with SARS-CoV-2 and dengue virus (DV) confection who died of a stroke 4 days after hospitalization (Figure 1). The authors illustrate how the overlapping symptoms of DV and SARS-CoV-2 (Table 1) can cause diagnostic confusion, both in honing a diagnosis and in determining the pathophysiology of the patient's vascular injury. The authors suggest that this case may provide clinicians guidance in detecting and managing DV/COVID-19 co-infected patients, although the outcomes and clinical course of such cases cannot be predicted by this case report alone.

ABSTRACT

Herein, we report a case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and dengue coinfection, presented as a fatal stroke in our hospital, in Sao Jose do Rio Preto, Sao Paulo State, a Brazilian city hyperendemic for dengue viruses and other arthropod-borne viruses (arboviruses) and currently facing a surge of SARS-CoV-2 cases. This case is the first described in the literature and contributes to the better understanding of clinical presentations of two important diseases in a tropical setting.

FIGURES

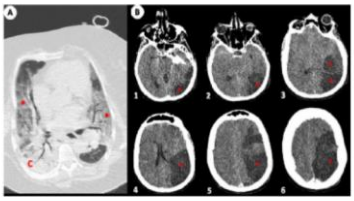


Figure 1. A) Lung computed tomographic imaging shown extensive areas of diffuse ground-glass attenuation (asterisks) related to basal and posterior consolidation process (C). B) Brain computed tomographic imaging evidenced an extensive hypodense injury (asterisk) involving the left cerebral and cerebellar hemispheres (1-6), inferring an area of subacute ischemic vascular injury, and edema in the left cerebral hemisphere, with a compressive effect and midline deviation

	Dengue	COVID-19
Main clinical characteristics	Fever, myalgia, headache, arthralgia, retroorbital pain, rash, fluid accumulation, abdominal pain, organ failure. Respiratory symptoms are not usual in mild presentation.	Fever, cough, myalgia, headache, nasal congestion, coryza, dyspnea, respiratory failure, thromboembolic events.
Diagnostic tools	RT-PCR by DENV positive. DENV NS1 antigen detection; anti-dengue IgM reagent	RT-PCR SARS-CoV-2
General laboratory findings	Increased hematocrit, leukopenia, lymphocytosis, decreased platelet count	Leukopenia, lymphopenia
Imaging tools	Chest X-ray or CT, abdominal US (fluid accumulation)	Chest CT (ground-glass animation; thromboembolic event)
	Brain images (CT or NMR) may contribute to identify neurological complications (stroke or bleeding)	Brain images (CT or NMR) may contribute to identify neurological complications (stroke or bleeding)

RT-PCR: reverse transcriptase polymerase chain reaction; DENV: dengue virus; NS1: non-structural protein type 1; IgM: Immunoglobulin type M; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; CT: computed tomography; US: ultrasonography; NMR: nuclear magnetic resonance

Table 2: Comparation of Dengue and COVID-19, according with clinical characteristics and complementary tools

ORTHOPEDICS

EFFICACY OF SURGICAL HELMET SYSTEMS FOR PROTECTION AGAINST COVID-19: A DOUBLE-BLINDED RANDOMISED CONTROL STUDY

Schaller G, Nayar SK, Erotocritou M, Overton A, Stelzhammer T, Berber O.. Int Orthop. 2020 Sep 8. doi: 10.1007/s00264-020-04796-3. Online ahead of print.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

A double-blinded RCT study conducted in London involved 35 participants (20 in experimental group while 15 received placebo) and found the Stryker Flyte Surgical Helmet, a type of sterile surgical helmet system (SSHS), was not effective in protecting against aerosolized particles, through analysis of aerosolized saccharin exposure causing the sensation of a sweet taste in the user (Figure 1; $p<0.0001$), and is thus ineffective at preventing transmission of COVID-19, suggesting SSHS should not be considered in the protocol of safely restarting elective surgical procedures.

ABSTRACT

PURPOSE: This study assesses whether sterile surgical helmet systems (SSHS) provide surgeons with additional protection from aerosol pathogens alongside their traditional role protecting against splash. There has been debate on whether to use such systems in reopening elective orthopaedic surgery during the current COVID-19 pandemic environment. METHODS: Thirty-five participants were enrolled in a double-blinded randomised controlled study investigating efficacy of the Stryker Flyte Surgical Helmet (Stryker Corporation, Kalamazoo, MI, USA) as protection against respiratory droplets. Wearing the SSHS in a fit testing hood, subjects were randomised to nebulised saccharin solution or placebo. Twenty were allocated to the saccharin group with 15 to placebo. Positive sweet taste represented a failure of the test. Taste tests were performed with the helmet fan turned on and off. RESULTS: SSHS did not prevent saccharin taste ($p < 0.0001$). Within the saccharin cohort, 40% recorded a positive taste with the fan on and 100% with the fan off. There was a statistically significant difference in mean time-to-taste saccharin ($p = 0.049$) comparing fan on (123.5 s) vs. off (62.6 s). CONCLUSIONS: SSHS do not protect against aerosol particulate and therefore are not efficacious in protection against COVID-19. The fan system employed may even increase risk to the surgeon by drawing in particulates as well as delay recognition of intraoperative cues, such as exhaust from diathermy, that point to respirator mask leak.

FIGURES

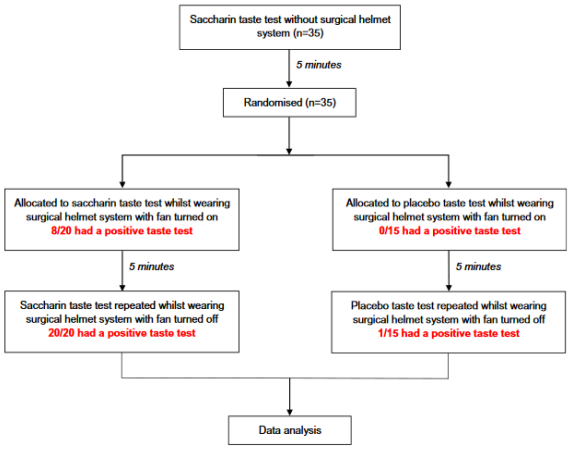


Figure 1. Flow diagram outlining results of saccharin testing

EVALUATION OF ORTHOGONAL TESTING ALGORITHM FOR DETECTION OF SARS-COV-2 IGG ANTIBODIES

Xu G, Emanuel AJ, Nadig S, Mehrotra S, Caddell BA, Curry SR, Nolte FS, Babic N.. Clin Chem. 2020 Sep 7:hvaa210. doi: 10.1093/clinchem/hvaa210. Online ahead of print.
Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

BLUF

Laboratory scientists from the Medical University of South Carolina evaluated test characteristics of a two-step serology-based orthogonal testing algorithm (OTA), wherein patients who tested positive via a first test (SARS-CoV-2 viral nucleocapsid protein IgG)(Table 1) were confirmed with a second test (SARS-CoV-2 viral spike IgG) (Table 2). Using 4,333 patient samples and SARS-CoV-2 PCR as gold-standard, they found second-line testing confirmed 80% of initially positive first-line tests and 11/26 (26%) previously diagnosed COVID-19 patients lacked detectable antibodies (Table 3). Authors suggest OTA may be useful for identification of patients with false-positive SARS-CoV-2 viral nucleocapsid protein IgG who require follow up testing, and that serologies may not reliably detect previous infection.

ABSTRACT

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody testing is an important tool in assessment of pandemic progress, contact tracing, and identification of recovered coronavirus disease 2019 (COVID-19) patients. We evaluated an orthogonal testing algorithm (OTA) to improve test specificity in these use cases. METHODS: A two-step OTA was applied where individuals who initially tested positive were tested with a second test. The first-line test, detecting IgG antibodies to the viral nucleocapsid protein was validated in 130 samples and the second-line test, detecting IgG antibodies to the viral spike protein in 148 samples. The OTA was evaluated in 4,333 clinical patient specimens. The seropositivity rates relative to the SARS-CoV-2 PCR positivity rates were evaluated from our entire patient population data (n = 5,102). RESULTS: The first-line test resulted in a clinical sensitivity of 96.4% (95% CI; 82.3% to 99.4%), and specificity of 99.0% (95% CI; 94.7% to 99.8%), whereas the second-line test had a sensitivity of 100% (95% CI; 87.7% to 100%) and specificity of 98.4% (95% CI; 94.2% to 99.5%). Using the OTA, 78/98 (80%) of initially positive SARS-CoV-2 IgG results were confirmed with a second-line test, while 11/42 (26%) of previously diagnosed COVID-19 patients had no detectable antibodies as long as 94 days post PCR diagnosis. CONCLUSION: Our results show that an OTA can be used to identify patients who require further follow-up due to potential SARS CoV-2 IgG false positive results. In addition, serological testing may not be sufficiently sensitive to reliably detect prior COVID-19 infection.

FIGURES

Table 1. Clinical sensitivity and specificity for Abbott ARCHITECT SARS-CoV-2 IgG test.

	Test positive	Test negative	Total
SARS-CoV-2 Infection	27	1	28
Asymptomatic/Pre-Pandemic	1	101	102
Total	28	102	**130**
% Sensitivity (95% CI)	96.4% (82.3% to 99.4%)		
% Specificity (95% CI)	99.0% (94.7% to 99.8%)		

Table 2. Clinical sensitivity and specificity for ELISA SARS-CoV-2 IgG test.

	Test positive	Test negative	Total
SARS-CoV-2 Infection	26	0	26
Asymptomatic/Pre-Pandemic	2	120	122
Total	28	120	**148**
% Sensitivity (95% CI)	100% (87.1% to 100%)		
% Specificity (95% CI)	98.4% (94.2% to 99.5%)		

Table 3. Verification of clinical sensitivity of 2-step orthogonal SARS-CoV-2 IgG serological testing on 5,102 clinical samples collected by MUSC from South Carolina residents for clinical testing April - late June 2020.

		SARS-CoV-2 PCR Results	
		PCR Positive ≥14 days prior to antibody test	No prior positive PCR
SARS-CoV-2 IgG Results	Positive	30	67
	Negative	11	4,977
	Discordant	1	16

DEVELOPMENTS IN DIAGNOSTICS

ULTRA-SENSITIVE SERIAL PROFILING OF SARS-COV-2 ANTIGENS AND ANTIBODIES IN PLASMA TO UNDERSTAND DISEASE PROGRESSION IN COVID-19 PATIENTS WITH SEVERE DISEASE

Ogata AF, Maley AM, Wu C, Gilboa T, Norman M, Lazarovits R, Mao CP, Newton G, Chang M, Nguyen K, Kamkaew M, Zhu Q, Gibson TE, Ryan ET, Charles RC, Marasco WA, Walt DR.. Clin Chem. 2020 Sep 8:hvaa213. doi: 10.1093/clinchem/hvaa213. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A case control study conducted in Boston, MA across various medical institutions utilizing a recently-developed Single Molecular Assay (Simoa) to quantitatively detect SARS-CoV-2 antigens (spike, S1, N) in 64 COVID-19 positive patients, 17 COVID-19 negative patients, and 34 pre-pandemic patients detected S1 and N antigens (Figure 1) in 41/64 COVID-19 patients with high S1 antigen concentration correlating with increased ICU admission rate (77%) and decreased time to intubation (<1 day) (Figure 5). These findings suggest viral fragments can enter the bloodstream, possibly via tissue damage secondary to COVID-19 infection, thus making these quantitative values a potentially effective way to detect presence of SARS-CoV-2 and estimate disease severity.

ABSTRACT

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 21 million people worldwide since August 16, 2020. Compared to PCR and serology tests, SARS-CoV-2 antigen assays are underdeveloped, despite their potential to identify active infection and monitor disease progression. METHODS: We used Single Molecule Array (Simoa) assays to quantitatively detect SARS-CoV-2 spike, S1 subunit, and nucleocapsid antigens in the plasma of coronavirus disease (COVID-19) patients. We studied plasma from 64 COVID-19 positive patients, 17 COVID-19 negative patients, and 34 pre-pandemic patients. Combined with Simoa anti-SARS-CoV-2 serological assays, we quantified changes in 31 SARS-CoV-2 biomarkers in 272 longitudinal plasma samples obtained for 39 COVID-19 patients. Data were analyzed by hierarchical clustering and were compared to longitudinal RT-PCR test results and clinical outcomes. RESULTS: SARS-CoV-2 S1 and N antigens were detectable in 41 out of 64 COVID-19 positive patients. In these patients, full antigen clearance in plasma was observed a mean +- 95%CI of 5 +- 1 days after seroconversion and nasopharyngeal RT-PCR tests reported positive results for 15 +- 5 days after viral antigen clearance. Correlation between patients with high concentrations of S1 antigen and ICU admission (77%) and time to intubation (within one day) was statistically significant. CONCLUSIONS: The reported SARS-CoV-2 Simoa antigen assay is the first to detect viral antigens in the plasma of COVID-19 positive patients to date. These data show that SARS-CoV-2 viral antigens in the blood are associated with disease progression, such as respiratory failure, in COVID-19 cases with severe disease.

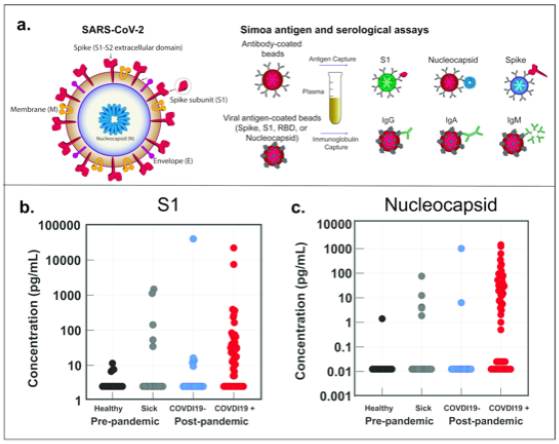


Figure 1. SARS-CoV-2 Antigen and anti-SARS-CoV-2 Immunoglobulin Detection in Plasma. a.) Schematic of Simoa detection of SARS-CoV-2 S1, spike, and N antigens and anti-SARS-CoV-2 immunoglobulins IgG, IgA, and IgM. Measurements for all antigens and immunoglobulins can be obtained from a single plasma sample (70 µL). b-c) Simoa SARS-CoV-2 antigen assay results for plasma samples collected from pre-pandemic healthy patients, pre-pandemic sick patients, COVID-19 negative patients, and COVID-19 positive patients. 41 of 64 COVID-19 positive patients show detectable b.) S1 and c.) N concentrations in plasma. Each data point represents the average of two replicate measurements

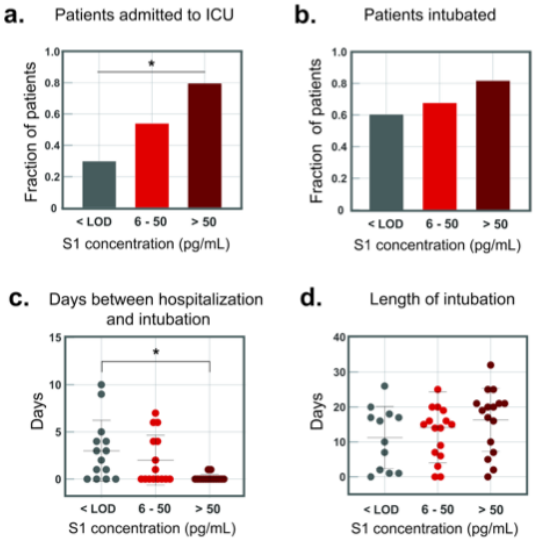


Figure 5. Indicators of disease severity based on S1 concentrations in plasma for 64 COVID-19 positive patients. COVID-19 positive patients were separated into three groups based on S1 concentrations. The cutoff between groups 2 and 3 (50 pg/mL, 0.65 pmol/L) was chosen as five standard deviations above the LOD. The fraction of patients admitted to the ICU or who were intubated was calculated for each group independently. a.) Fraction of COVID-19 positive patients who were immediately admitted to the ICU upon presentation to the hospital. b.) Fraction of COVID-19 positive patients who were intubated during hospitalization. c.) Days between date of presentation to the hospital and intubation date for intubated COVID-19 positive patients. d.) The length of intubation for intubated COVID-19 positive patients. For all plots, significance indicated by the asterisks (P value <0.05).

POTENTIAL ROLE OF SUBCUTANEOUS TOCILIZUMAB INJECTIONS IN PATIENTS WITH COVID-19 ASSOCIATED PNEUMONIA

Greco G, Ripamonti D, Binda F, Fabretti F, Grazioli L, Rizzi M.. J Med Virol. 2020 Sep 8. doi: 10.1002/jmv.26494. Online ahead of print.

Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A case series conducted at ASST Papa Giovanni XXIII in Bergamo, Italy from March 20 - April 5, 2020 found that among 24 COVID-19 positive patients (Table 1) presenting with fever, pneumonia, and IL-6 elevation, all patients had fever resolution within 48 hours of intravenous or subcutaneous tocilizumab (humanized anti-IL-6 receptor antibody) treatment and significantly reduced CRP levels from an average of 17.1 to 0.8 ($p<0.05$), with 20 patients stable enough to be discharged. Fifteen of the 24 patients experienced adverse events following treatment such as septic shock, AST/ALT elevations, thrombocytopenia, and neutropenia, though no patients died in this study group. This study suggests that further randomized clinical trials are needed to assess the efficacy and safety of tocilizumab treatment in hospitalized COVID-19 patients with elevated IL-6 and associated pneumonia.

ABSTRACT

Guaraldi et al. found a significant reduction in risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia who were treated with either I.V. or S.C. tocilizumab and standard of care, compared with those treated with standard of care only. This article is protected by copyright. All rights reserved.

FIGURES

Table 1: Baseline patients' characteristics

	N. (%)
Patients	24
Age, mean (range), years	60 (35-78)
Gender	
Male	18 (75.0)
Comorbidities	
Neoplasia	1 (4.2)
Diabetes	5 (20.8)
Cardiovascular disease	2 (8.3)
Hypertension	7 (29.2)
Respiratory disease	3 (12.5)
Renal disease	2 (8.3)
Metabolic disease	7 (29.2)
Symptoms	
Fever	24 (100)
Dyspnoea	24 (100)
Cough	15 (62.5)
Asthenia	8 (33.3)
Sore throat	1 (4.2)
Headache	3 (12.5)
Confusion	4 (16.7)
Gastrointestinal symptoms	11 (45.8)
Time to hospitalization mean (range), days	12 (7-21)
Concomitant medications	
darunavir/cobicistat	15 (62.5)
hydroxycloroquine	23 (95.8)
azithromycin	24 (100)
high dose steroids	18 (75.0)
low-weight heparin	21(87.5)
other anticoagulants	1 (4.2)

Oxygen support

	Baseline	192h
Nasal cannula	0 (0)	5 (20.8)
VentiMask	2 (8.3)	8 (33.3)
Non-rebreathing mask	8 (33.3)	2 (8.3)
CPAP	13 (54.2)	2 (8.3)
Oro-tracheal intubation	1 (4.2)	7 (29.2)

cPAP: continuous Positive Airway Pressure.

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