The Daily COVID-19 Literature Surveillance Summary

March 01, 2021

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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

Transmission & Prevention

- Are there issues with SARS-COV-2 vaccines and autoimmune diseases? In this review, authors from various institutions in Bulgaria detailed the current research regarding the effectiveness and safety of different types of vaccines in the setting of patients with autoimmune inflammatory diseases (AIIDs). They reviewed vaccines that use whole virus, protein subunit, viral vector, and nucleic acids, concluding that although more research is warranted, they believe vaccinations themselves do not pose more danger than the natural infections they are used to combat, and that the risk of COVID-19 vaccines should not lead to delay in administration to AIID patients.

Management

- Anticoagulation and aspirin may reduce in-hospital mortality in COVID-19 patients. A retrospective cohort study by researchers at Yale School of Medicine of 2,785 hospitalized COVID-19 positive adults treated with either prophylactic-dose anticoagulation or intermediate-dose anticoagulation found that intermediate-dose anticoagulation was associated with a lower incidence of in-hospital death (hazard ratio 0.518 [0.308-0.872]), as was aspirin compared to no anti-platelet therapy (hazard ratio 0.522 [0.336-0.812]), suggesting that anticoagulation and anti-platelet therapy in hospitalized COVID-19 patients is an important method of reducing in-hospital death.

Adjusting Practice During COVID-19

- Comparing methodological and reporting quality of COVID-19 and other research from the first wave of the pandemic shows decreasing quality. A team of experienced medical researchers from the University of Glasgow compared the quality of COVID-19 research to non-COVID-19 related research published between December 2019 and May 2020. They found non-COVID-19 related papers were more likely to have a low risk of bias (OR 6.3, 95%CI 2.9 to 14.0; $p < 0.001$) and adhere to reporting guidelines (84% [95%CI 81 to 87] vs 71% [95%CI 66 to 77]) compared to COVID-19 research. Authors suggest COVID-19 related research early in the pandemic was of lower methodological quality, and emphasizes that compromising quality is not scientifically acceptable, even during a pandemic.

R&D: Diagnosis & Treatments

- Is SARS-CoV-2 antigen-detecting rapid test with self-collected nasal swab a good test? Infectious disease experts from Charité University Hospital in Berlin compare supervised, self-collected nasal mid-turbinate (NMT) swab samples with health care worker (professional)-collected nasopharyngeal (NP) swab samples in 303 adults deemed to be at high risk for SARS-CoV-2 infection according to clinical suspicion. They obtained no invalid results and found two patients were detected by NP but not by NMT sampling while no patients were detected by NMT sampling only (positive percent agreement: 90.6% [CI 75.8-96.8]; negative percent agreement: 99.2% [CI 97.2-99.8]). Authors suggest supervised nasal self-sampling is a reliable alternative to professional nasopharyngeal sampling when using a WHO-listed SARS-CoV-2 antigen-detecting rapid test.

- Shrinky-Dink© electrodes can detect the SARS-CoV-2 spike protein in saliva. American and Brazilian biotechnology experts collaborate on this proof of mechanism research that demonstrates how the electrodes from a children's toy can be modified to detect SARS-CoV-2 spike protein (S1) in saliva. Researchers utilized an aptamer-based electrochemical assay made from wrinkled electrodes in the Shrinky-Dink toy designed to bind specifically to the receptor binding domain of SARS-CoV-2 spike protein, finding this was efficacious for detection of S1 in saliva. Further studies are needed to validate at different probe densities and to identify the whole virus instead of just S1. These findings suggest potential to increase accessibility of SARS-CoV-2 detection with low-cost screening materials and expansion for wide-range detection and analyses for future epidemics.

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DEVELOPMENTS IN TRANSMISSION & PREVENTION

SARS-COV-2 VACCINES AND AUTOIMMUNE DISEASES AMIDST THE COVID-19 CRISIS

Velikova T, Georgiev T.. Rheumatol Int. 2021 Jan 30. doi: 10.1007/s00296-021-04792-9. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

In this review, authors from various institutions in Bulgaria detailed the current research published from January 2020 through January 2021 regarding the effectiveness and safety of different types of vaccines in the setting of patients with autoimmune inflammatory diseases (AIIDs). They reviewed vaccines that use whole virus, protein subunit, viral vector, and nucleic acids, concluding that although more research is warranted, they believe vaccinations themselves do not pose more danger than the natural infections they are used to combat, and that the risk of COVID-19 vaccines should not lead to delay in administration to AIID patients.

ABSTRACT

Coronavirus disease 2019 (COVID-19) pandemic has become challenging even for the most durable healthcare systems. It seems that vaccination, one of the most effective public-health interventions, presents a ray of hope to end the pandemic by achieving herd immunity. In this review, we aimed to cover aspects of the current knowledge of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines and vaccine candidates in the light of autoimmune inflammatory diseases (AIIDs) and to analyze their potential in terms of safety and effectiveness in patients with AIIDs. Therefore, a focused narrative review was carried out to predict the possible implications of different types of SARS-CoV-2 vaccines which confer distinct immune mechanisms to establish immune response and protection against COVID-19: whole virus (inactivated or weakened), viral vector (replicating and non-replicating), nucleic acid (RNA, DNA), and protein-based (protein subunit, virus-like particle). Still, there is uncertainty among patients with AIIDs and clinicians about the effectiveness and safety of the new vaccines. There are a variety of approaches towards building a protective immunity against SARS-CoV-2. Only high-quality clinical trials would clarify the underlying immunological mechanisms of the newly implemented vaccines/adjuvants in patients living with AIIDs.

CAN WE PROTECT PREGNANT WOMEN AND YOUNG INFANTS FROM COVID-19 THROUGH MATERNAL IMMUNIZATION?

Munoz FM.. JAMA Pediatr. 2021 Jan 29. doi: 10.1001/jamapediatrics.2021.0043. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

An infectious disease physician from the Baylor College of Medicine reports on a study published in JAMA Pediatrics in January 2021 which found that vaccination occurring in the early to late third trimester may provide protection for pregnant patients, while the potential for transplacental transfer of antibodies to infants remains unclear. Further research is needed to ascertain the feasibility of maternal immunization as protective for infants.

SUMMARY

- the large study being analyzed by this paper includes 1714 pregnant women who delivered newborns from April to August 2020

- Of the 83 women (6%) with detectable antibodies, most infants (87%) possessed detectable antibodies at birth.

- transplacental transfer appears to be efficient, without or without the presence of symptoms from COVID-19 infection.

- factors which remain to be studied include: how long antibodies last when transferred, efficacy against COVID-19, long-term effects on immunity, and the regimen for infants necessary.

INTERMEDIATE-DOSE ANTICOAGULATION, ASPIRIN, AND IN-HOSPITAL MORTALITY IN COVID-19: A PROPENSITY SCORE-MATCHED ANALYSIS

Meizlish ML, Goshua G, Liu Y, Fine R, Amin K, Chang E, DeFilippo N, Keating C, Liu Y, Mankbadi M, McManus D, Wang SY, Price C, Bona RD, Ochoa Chaar CI, Chun HJ, Pine AB, Rinder HM, Siner JM, Neuberg DS, Owusu KA, Lee AI.. Am J Hematol. 2021 Jan 21. doi: 10.1002/ajh.26102. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A retrospective cohort study by researchers at Yale School of Medicine of 2785 hospitalized COVID-19 positive adults treated with either prophylactic-dose anticoagulation or intermediate-dose anticoagulation found that intermediate-dose anticoagulation was associated with a lower incidence of in-hospital death (hazard ratio 0.518 [0.308-0.872]), as was aspirin compared to no anti-platelet therapy (hazard ratio 0.522 [0.336-0.812]), suggesting that anticoagulation and anti-platelet therapy in hospitalized COVID-19 patients is an important method of reducing in-hospital death.

ABSTRACT

Thrombotic complications occur at high rates in hospitalized patients with COVID-19, yet the impact of intensive antithrombotic therapy on mortality is uncertain. We examined in-hospital mortality with intermediate- compared to prophylactic-dose anticoagulation, and separately with in-hospital aspirin compared to no antiplatelet therapy, in a large, retrospective study of 2785 hospitalized adult COVID-19 patients. In this analysis, we established two separate, nested cohorts of patients (1) who received intermediate- or prophylactic-dose anticoagulation ("anticoagulation cohort", N = 1624), or (2) who were not on home antiplatelet therapy and received either in-hospital aspirin or no antiplatelet therapy ("aspirin cohort", N = 1956). To minimize bias and adjust for confounding factors, we incorporated propensity score matching and multivariable regression utilizing various markers of illness severity and other patient-specific covariates, yielding treatment groups with well-balanced covariates in each cohort. The primary outcome was cumulative incidence of in-hospital death. Among propensity score-matched patients in the anticoagulation cohort (N = 382), in a multivariable regression model, intermediate-compared to prophylactic-dose anticoagulation was associated with a significantly lower cumulative incidence of in-hospital death (hazard ratio 0.518 [0.308-0.872]). Among propensity-score matched patients in the aspirin cohort (N = 638), in a multivariable regression model, in-hospital aspirin compared to no antiplatelet therapy was associated with a significantly lower cumulative incidence of in-hospital death (hazard ratio 0.522 [0.336-0.812]). In this propensity score-matched, observational study of COVID-19, intermediate-dose anticoagulation and aspirin were each associated with a lower cumulative incidence of in-hospital death.

FOLLOWING THE SCIENCE? COMPARISON OF METHODOLOGICAL AND REPORTING QUALITY OF COVID-19 AND OTHER RESEARCH FROM THE FIRST WAVE OF THE PANDEMIC

Quinn TJ, Burton JK, Carter B, Cooper N, Dwan K, Field R, Freeman SC, Geue C, Hsieh PH, McGill K, Nevill CR, Rana D, Sutton A, Rowan MT, Xin Y.. BMC Med. 2021 Feb 23;19(1):46. doi: 10.1186/s12916-021-01920-x.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

A team of experienced medical researchers from the University of Glasgow compared the quality (see summary) of COVID-19 research to non-COVID-19 related research published between December 2019 and May 2020 (Table 1, Figure 1). They found non-COVID-19 related papers were more likely to have a low risk of bias (OR 6.3, 95%CI 2.9 to 14.0; p < 0.001)(Figure 4) and adhere to reporting guidelines (84% [95%CI 81 to 87] vs 71% [95%CI 66 to 77]) compared to COVID-19 research. Authors suggest COVID-19 related research early in the pandemic was of lower methodological quality, and emphasizes that compromising quality is not scientifically acceptable, even during a pandemic.

SUMMARY

Methodological quality defined as risk of bias, which took into account "journal, study design, whether the paper was identified as a 'Brief Report' or equivalent, the exposure of interest (or intervention, or index test), covid-19 status, the total 'n' included in the study at baseline (for a systematic review this was taken as the number of included papers), follow-up (time from first measure to last measure for primary outcome, quantified in weeks) and funding source (academic or industry)." (Table 1)

Reporting quality was defined as reporting guideline compliance

FIGURES

Table 1 Tools used to assess quality (risk of bias) and reporting

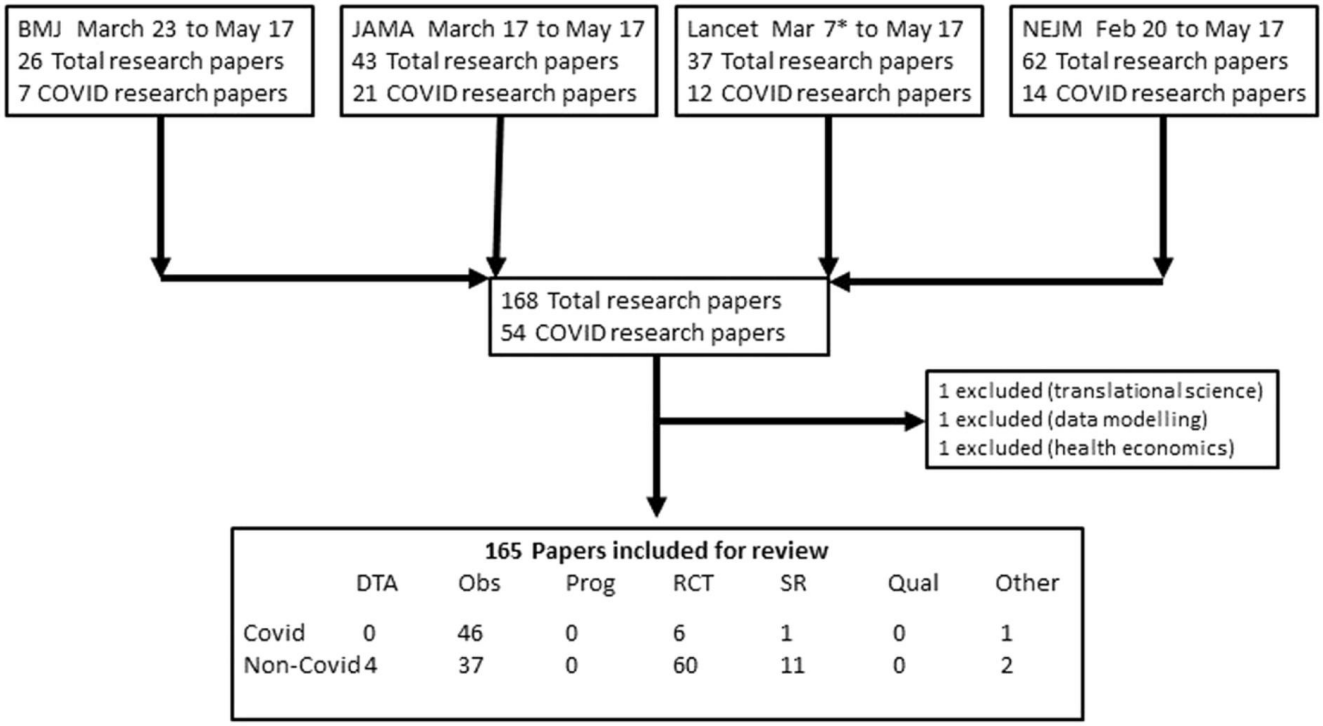
From: Following the science? Comparison of methodological and reporting quality of covid-19 and other research from the first wave of the pandemic

Design	Quality (risk of bias)	Domains assessed	Reporting
Controlled trial	Cochrane RoB	Randomisation, allocation, blinding (participants), blinding (outcomes), incomplete outcomes, selective reporting, other	CONSORT
Observational	NHLBI	Question, population, exposure, outcomes, confounding, other	STROBE
Test accuracy	QUADAS2	Patient selection, index test, reference standard, flow and timing, generalisability, other	STARD
Systematic review	AMSTAR2	Design and protocol, search strategy, paired extraction, inclusion/exclusion, risk of bias, meta-analysis, conflicts of interest, other	PRISMA
Qualitative	CASP	Design, recruitment, data collection, relationships, analysis, other	COREQ
Prognosis	PROBAST	Participants, predictors, outcomes, analysis, generalisability, other	TRIPOD

Table 1 Tools used to assess quality (risk of bias) and reporting

Fig. 1

From: Following the science? Comparison of methodological and reporting quality of covid-19 and other research from the first wave of the pandemic



PRISMA flow diagram describing search strategy and inclusion. Flow diagram illustrating literature search and results. NB The Lancet published two data modelling covid-19 research papers in February 2020; these did not meet our definition of clinical research and so first paper included was March

Fig. 2 Comparing published covid-19 and non-covid research using the classical ‘evidence pyramid’ hierarchy. NB For this illustration, the category ‘observational’ is further divided into cases series and case control/cohort. Not all of our chosen research designs feature on the classical evidence hierarchy pyramid. All differences are significant at P < 0.05

Fig. 4

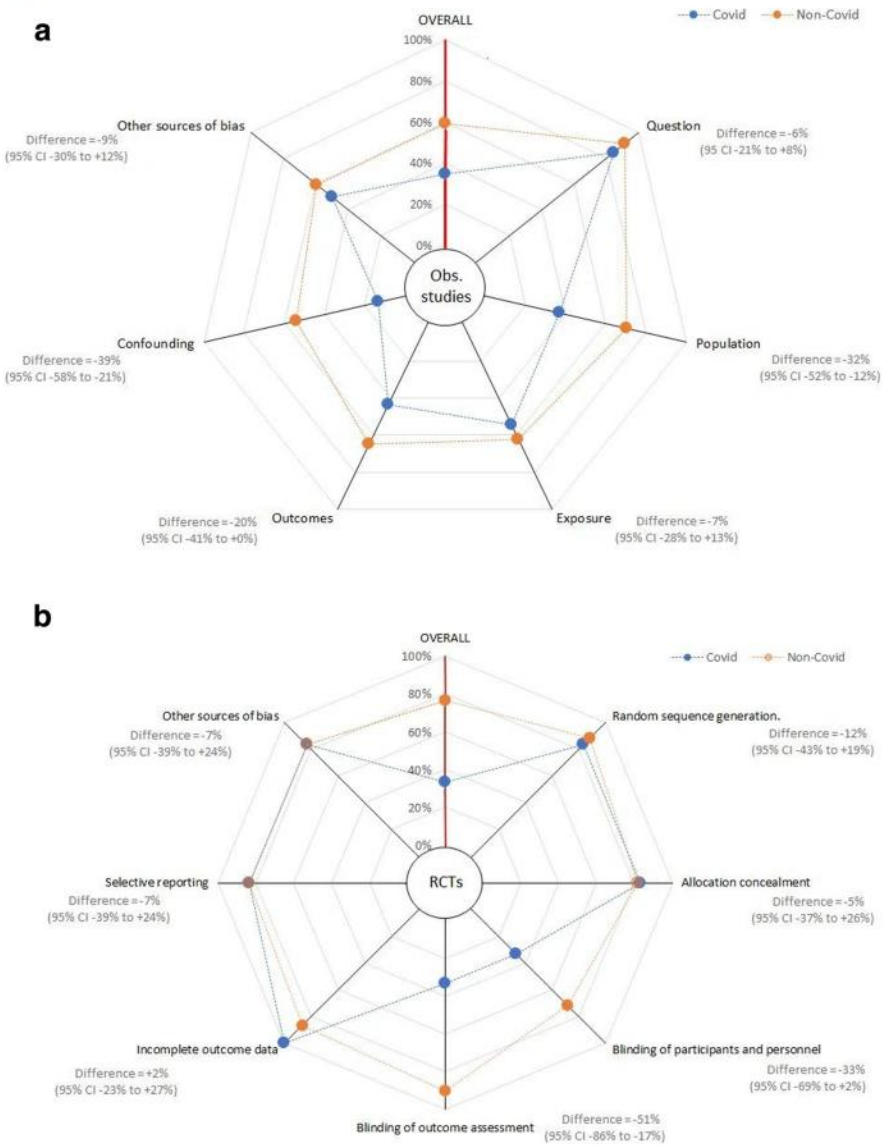


Fig. 4 a, b Modified star plots, describing methodological quality (risk of bias) overall and for each domain of the risk of bias assessment tool for differing study methods. a Randomised controlled trials (using Cochrane RoB1 tool). b Observational studies (using NHLBI tool). Blue spokes represent covid-19 studies and orange spokes represent non-covid 19 studies. RCTS, randomised controlled trials; Obs studies, observational studies

THROMBOCYTOPENIA FOLLOWING PFIZER AND MODERNA SARS/COV-2 VACCINATION

Lee EJ, Cines DB, Gernsheimer T, Kessler C, Michel M, Tarantino MD, Semple JW, Arnold DM, Godeau B, Lambert MP, Bussel JB.. Am J Hematol. 2021 Feb 19. doi: 10.1002/ajh.26132. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

A literature review conducted at the New York Presbyterian Hospital during early 2021 by the Division of Hematology found that, when identifying case reports of patients with thrombocytopenia using the Vaccine Adverse Events Reporting System, the incidence of Immune Thrombocytopenia (ITP) following COVID-19 vaccination is comparable to the incidence rate in the general population (50,000 vs. 80,000 new cases per year respectively when adjusted for the population that has been vaccinated). They suggest these results may inform treatment of ITP but should not be used for adjustments in diagnosis of ITP or COVID-19 vaccine administration.

GENERAL SURGERY

MEASURING THE IMPACT OF DELAYED ACCESS TO ELECTIVE CHOLECYSTECTOMY THROUGH PATIENT'S COST-UTILITY: AN OBSERVATIONAL COHORT STUDY

Karimuddin A, Melina Albanese C, Crump T, Liu G, Sutherland JM.. Int J Qual Health Care. 2021 Jan 25:mzab018. doi: 10.1093/intqhc/mzab018. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Researchers from the University of British Columbia conducted a retrospective analysis of a longitudinal sample of 195 patients in Vancouver, Canada who underwent elective cholecystectomy and completed patient-reported outcomes (PROs) measuring their health status before and after their procedure (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), in order to determine the utility of delaying such procedures during the pandemic. They found that a delay in surgery of 12 months resulted in 6.4% loss of quality of life, increasing to 21.5% if the patient was over 70 years of age (Figure 1), emphasizing the importance of some elective surgeries in the face of COVID-19 restrictions at some hospitals and suggesting that the procedures may be worth the risk in some instances.

ABSTRACT

BACKGROUND: Deferral of surgeries due to COVID-19 has negatively affected access to elective surgery and may have deleterious consequences for patient's health. Delays in access to elective surgery are not uniform in their impact on patients with different attributes. The objective of this study is to measure the change in patient's cost utility due to delayed elective cholecystectomy. METHODS: This study is based on retrospective analysis of a longitudinal sample of participants that have had elective cholecystectomy and completed the EQ-5D(3L) measuring health status preoperatively and postoperatively. Emergent cases were excluded. Patients younger than 19 years of age, unable to communicate in English, or residing in a long-term care facility were ineligible.Quality adjusted life years attributable to cholecystectomy were calculated by comparing health state utility values between the pre- and post-operative time points. The loss in quality adjusted life years due to delayed access was calculated under four assumed scenarios regarding the length of the delay. The mean cost per quality adjusted life years are shown for the overall sample and by sex and age categories. RESULTS: Among the 646 eligible patients, 30.1% of participants (N=195) completed their preoperative and postoperative EQ-5D(3L). A delay of 12 months resulted in a mean loss of 6.4%, or 0.117, of the quality adjusted life years expected without the delay. Among patients older than 70 years of age, a 12-month delay in their surgery corresponded with a 25.1% increase in the cost per quality adjusted life years, from $10,758 to $13,463. CONCLUSIONS: There is a need to focus on minimizing loss of quality of life for patients affected by delayed surgeries. Faced with equal delayed access to elective surgery, triage may need to prioritize older patients to maximize their health over their remaining life years.

Figure 1. Illustration of the impact of delayed surgery and gain in health utility.

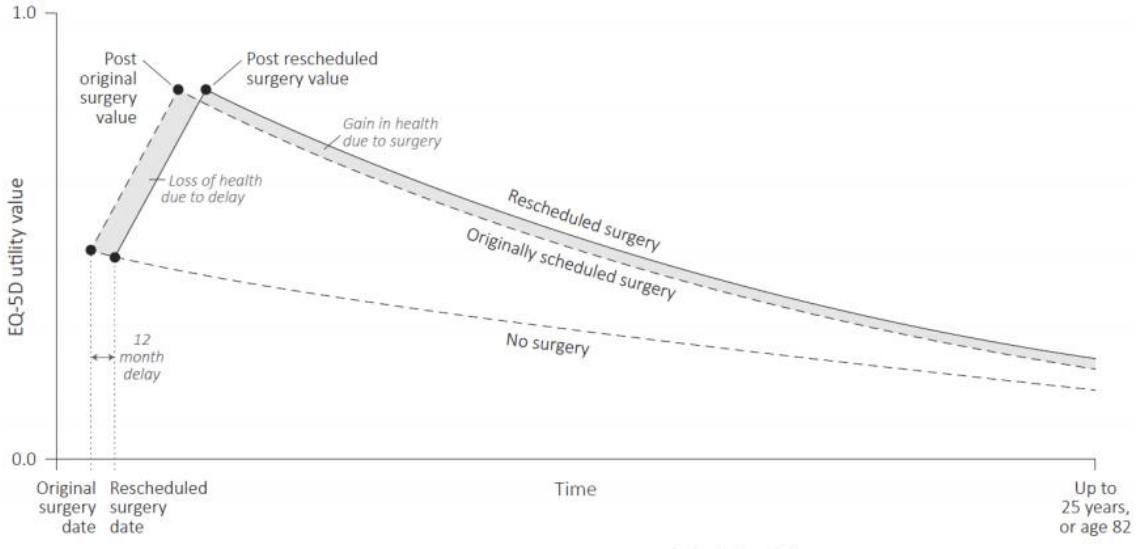


Figure 1. Illustration of the impact of delayed surgery and gain in health utility.

HEAD-TO-HEAD COMPARISON OF SARS-COV-2 ANTIGEN-DETECTING RAPID TEST WITH SELF-COLLECTED NASAL SWAB VERSUS PROFESSIONAL-COLLECTED NASOPHARYNGEAL SWAB

Lindner AK, Nikolai O, Kausch F, Wintel M, Hommes F, Gertler M, Krüger LJ, Gaeddert M, Tobian F, Lainati F, Köppel L, Seybold J, Corman VM, Drosten C, Hofmann J, Sacks JA, Mockenhaupt FP, Denkinger CM.. Eur Respir J. 2021 Feb 25:2003961. doi: 10.1183/13993003.03961-2020. Online ahead of print.
Level of Evidence: 2 - Individual cross sectional studies with consistently applied reference standard and blinding

BLUF

Infectious disease experts from Charité University Hospital in Berlin compare supervised, self-collected nasal mid-turbinate (NMT) swab samples with health care worker (professional)-collected NP swab samples in 303 adults deemed to be at high risk for SARS-CoV-2 infection according to clinical suspicion (see summary). They obtained no invalid results, and found two patients were detected by NP but not by NMT sampling while no patients were detected by NMT sampling only (positive percent agreement: 90.6% [CI 75.8-96.8]; negative percent agreement: 99.2% [CI 97.2-99.8])(Table 1). Authors suggest supervised nasal self-sampling is a reliable alternative to professional nasopharyngeal sampling when using a WHO-listed SARS-CoV-2 antigen-detecting rapid test.

SUMMARY

WHO-listed SARS-CoV-2 Ag-RDT was used against the reference standard RT-PCR collected from a NP/oropharyngeal (OP) swab.

Participants were excluded if one or both of the swabs for the Ag-RDT or the RT-PCR reference standard could not be obtained.

TABLE 1 Antigen-detecting RDT results with a supervised self-collected nasal mid-turbinate swab and with a professional-collected nasopharyngeal (NP) swab in RT-PCR positive patients from combined oro-/nasopharyngeal swab. CT-values and viral load (in descending order) of the paired RT-PCR samples are shown, as well as the duration of symptoms per patient. The positive percent agreement between AN and NP samples on Ag-RDT, as well as the respective sensitivities compared to RT-PCR are shown.

No.	NMT swab self-collected SD Q Ag-RDT	NP swab prof.-collected SD Q Ag-RDT	OP/NP swab RT-PCR		Symptom duration (days)
			CT value	Viral load[3]	
1	pos (+++)	pos (+++)	17.33[1]	9.59	2
2	pos (++)	pos (+++)	17.86[1]	9.43	1
3	pos (+++)	pos (+++)	18.01[1]	9.38	1
4	pos (++)	pos (+++)	18.31[1]	9.29	3
5	pos (+++)	pos (+++)	18.40[1]	9.27	3
6	pos (+++)	pos (+++)	18.76[1]	9.16	4
7	pos (+++)	pos (+++)	18.77[1]	9.16	5
8	pos (+++)	pos (+++)	18.78[1]	9.16	5
9	pos (+++)	pos (+++)	19.05[1]	9.08	3
10	pos. (+++)	pos. (+++)	19.40[1]	8.97	2
11	neg.	pos (+++)	19.66[1]	8.90	1
12	pos (+++)	pos (+++)	20.32[1]	8.70	3
13	pos (+++)	pos (+++)	17.81[2]	8.68	4
14	pos (++)	pos (+++)	20.44[1]	8.67	2
15	pos (++)	pos (++)	20.54[1]	8.63	5
16	pos (+++)	pos (+++)	21.09[1]	8.47	4
17	pos (+++)	pos (+)	18.62[2]	8.44	4
18	pos (+)	pos (++)	21.87[1]	8.24	7
19	pos (++)	pos (+++)	19.34[2]	8.23	5
20	pos (++)	pos (+++)	22.05[1]	8.19	2
21	pos (+++)	pos (+++)	19.47[2]	8.19	6
22	pos (+++)	pos (+++)	22.60[1]	8.03	6
23	pos (+++)	pos (++)	23.66[1]	7.71	6
24	pos (+)	pos (++)	26.42[1]	6.90	5
25	pos (+++)	pos (+++)	26.77[1]	6.79	5
26	neg.	neg.	24.25[2]	6.78	10
27	pos (++)	pos (+++)	24.77[2]	6.62	4
28	pos (+++)	pos (++)	25.29[2]	6.46	2
29	pos (+)	pos (++)	29.33[1]	6.03	5
30	neg.	neg.	29.56[1]	5,97	3
31	neg.	neg.	29.95[1]	5.85	3
32	pos (+)	pos (+)	30.25[1]	5.76	4
33	neg.	neg.	27.81[2]	5.72	8
34	pos (++)	pos (+)	31.20[1]	5.48	8
35	neg.	pos (+)	31.61[1]	5.36	10
36	neg.	neg.	32.58[1]	5.07	10
37	neg.	neg.	32.86[1]	4.99	2
38	neg.	neg.	34.62[1]	4.47	7
39	neg.	neg.	35.53[1]	4.20	14
	Sensitivity 29/39 (74.4%)	**Sensitivity** 31/39 (79.5%)			
	Positive percent agreement[4] 90.6% (CI 75.8-96.8)				

[1] Roche Cobas SARS-CoV-2 assay (E-gene, T2 target)
[2] TibMolbiol assay, E-gene target.
[3] $\log_{10}$ RNA SARS-CoV2/swab
[4] including 2 false positives on NMT and 1 on NP

Abbreviations: No., patient number; SD Q, STANDARD Q COVID-19 Ag Test (SD Biosensor); Ag-RDT, antigen-detecting rapid diagnostic test; NMT, nasal mid-turbinate; NP, nasopharyngeal; OP, oropharyngeal; CT, cycle threshold; RT-PCR, reverse transcription-polymerase chain reaction; neg., negative; pos (+), weak positive; pos. (++), positive; pos. (+++), strong positive.

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CD8(+) T CELLS PREDICTED THE CONVERSION OF COMMON COVID-19 TO SEVERE

Liu L, Chen Z, Du Y, Gao J, Li J, Deng T, Chen C, Wang L, Yang Y, Liu C.. Sci Rep. 2021 Jan 26;11(1):2169. doi: 10.1038/s41598-021-81732-4.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A retrospective regression analysis of 408 COVID-19 patients conducted by researchers from Yunnan and Hubei, China found that elevated CD8+ T cells (p=0.010) and lactate (p=0.042) served as independent risk factors for developing severe infection (Table 4). This suggests that these two markers should be monitored early in the disease process, but due to the limited sample size of this study, more research is necessary to support these findings.

SUMMARY

- 408 patients, all with mild or normal disease severity at the time of diagnosis, were accepted, and ruled in using specific values of viral load (a CT value less than 37 on real-time PCR).

- In the 6-10 days following diagnosis, 60 patients developed a severe infection.

- From January 20, to March 15, 2020, CD8 T cells, lactate, CD4, Albumin, Iron, and Calcium were measured every 3 to 4 days (Table 2).

- Proposed mechanisms for CD8 T cell depletion include potential death of virally infected cells in inflamed tissues during infection.

ABSTRACT

To evaluate the predictive effect of T-lymphoid subsets on the conversion of common covid-19 to severe. The laboratory data were collected retrospectively from common covid-19 patients in the First People's Hospital of Zaoyang, Hubei Province, China and the Third People's Hospital of Kunming, Yunnan Province, China, between January 20, 2020 and March 15, 2020 and divided into training set and validation set. Univariate and multivariate logistic regression was performed to investigate the risk factors for the conversion of common covid-19 to severe in the training set, the prediction model was established and verified externally in the validation set. 60 (14.71%) of 408 patients with common covid-19 became severe in 6-10 days after diagnosis. Univariate and multiple logistic regression analysis revealed that lactate (P = 0.042, OR = 1097.983, 95% CI 1.303, 924,798.262) and CD8+ T cells (P = 0.010, OR = 0.903, 95% CI 0.835, 0.975) were independent risk factors for general type patients to turn to severe type. The area under ROC curve of lactate and CD8+ T cells was 0.754 (0.581, 0.928) and 0.842 (0.713, 0.970), respectively. The actual observation value was highly consistent with the prediction model value in curve fitting. The established prediction model was verified in 78 COVID-19 patients in the verification set, the area under the ROC curve was 0.906 (0.861, 0.981), and the calibration curve was consistent. CD8+ T cells, as an independent risk factor, could predict the transition from common covid-19 to severe.

Variable	All (408)	Mild and common group (348)	Severe and critical group (60)	P	Z
WBC	4.53 (3.22, 6.06)	4.44 (3.19, 5.91)	5.09 (4.10, 7.56)	0.078	−1.762
N	2.83 (2.03, 4.33)	2.70 (1.93, 3.88)	3.86 (2.81, 6.44)	0.081	−1.743
L	0.93 (0.68, 1.45)	0.97 (0.70, 1.49)	0.79 (0.58, 1.14)	0.021	−2.305
RBC	4.46 (4.03, 4.94)	4.45 (4.07, 4.93)	4.46 (3.99, 5.04)	0.502	−0.671
HB	136 (122, 149)	136 (122, 151)	136 (116, 149)	0.667	−0.43
BPC	168 (126, 240)	171 (140, 245)	134 (123, 226)	0.169	−1.375
CRP	16.27 (11.15, 30.29)	16.27 (11.00, 28.13)	16.28 (11.20, 48.70)	0.535	−0.62
HCRP	4.74 (4.72, 4.76)	4.75 (4.73, 4.76)	4.75 (4.74, 4.76)	0.542	−0.61
PCT	0.05 (0.04, 0.53)	0.05 (0.04, 0.05)	0.05 (0.05, 0.08)	0.164	−1.39
PH	7.41 (7.40, 7.43)	7.41 (7.40, 7.43)	7.42 (7.40, 7.44)	0.321	−0.993
pCO2	38 (35, 40)	38 (35, 40)	37 (33, 40)	0.493	−0.685
pO2	84 (74, 92)	84 (77, 93)	86 (56, 89)	0.593	−1.392
Lac	2.1 (1.9, 2.2)	2.1 (1.9, 2.2)	2.2 (1.8, 2.8)	0.408	−0.827
Pao2	106 (87, 121)	103 (81, 116)	132 (107, 173)	0.001	−3.251
A-AdO2	21 (5, 43)	20 (4, 39)	48 (20, 70)	0.005	−2.83
paO2/Pao2	0.92 (0.88, 0.99)	0.92 (0.90, 1.01)	0.68 (0.63, 0.89)	0.004	−2.91
LA	0.35 (0.09, 0.60)	0.34 (0.00, 0.57)	0.6 (0.1, 1.3)	0.014	−2.463
HCO3	23.7 (22.6, 24.5)	23.6 (22.6, 24.4)	23.7 (23.5, 24.8)	0.587	−0.543
SaO2	94 (93, 97)	94 (93, 96)	96 (90, 97)	0.413	−0.818
ESR	22 (10, 42)	22 (8, 35)	30 (18, 61)	0.075	−1.782
PT	10.4 (9.3, 11.5)	10.4 (9.0, 11.5)	10.5 (9.2, 12.1)	0.548	−0.6
PT (%)	129.92 (118, 142)	129.92 (129.92, 142.5)	129 (125, 130)	0.605	−0.517
INR	0.93 (0.78, 1.05)	0.93 (0.77, 1.04)	0.92 (0.79, 1.09)	0.684	−0.406
APTT	30.90 (27.67, 33.90)	30.50 (27.60, 33.80)	31.80 (28.67, 35.70)	0.314	−1.006
TT	14.10 (13.27, 14.92)	14.04 (12.89, 14.90)	14.43 (13.90, 15.40)	0.143	−1.465
FIB	3.12 (2.63, 4.73)	3.12 (2.61, 4.74)	3.52 (2.81, 4.61)	0.62	−0.496
FDP	1.66 (1.36, 1.87)	1.66 (1.36, 1.87)	1.65 (1.38, 2.49)	0.419	−0.809
TB	10.1 (7.9, 16.4)	10.1 (8.1, 15.4)	11.3 (7.0, 19.3)	0.951	−0.061
ALT	22.2 (15.5, 34.0)	22.3 (16.0, 36.0)	20.0 (14.7, 28.8)	0.347	−0.94
AST	27 (21, 34)	27 (22, 34)	25 (19, 34)	0.603	−0.52
GGT	27 (17, 41)	27.4 (17.2, 38.8)	36.8 (17.9, 63.4)	0.395	−0.85
ALP	66 (54, 80)	66 (54, 81)	66 (52, 70)	0.461	−0.737
ALB	41.1 (36.7, 46.0)	41.9 (38.6, 46.8)	36.5 (34.3, 40.2)	0.004	−2.868
GLO	29.5 (26.0, 32.6)	29.6 (25.9, 31.7)	28.2 (26.0, 36.4)	0.464	−0.732
PALB	235 (210, 263)	236 (211, 261)	245 (188, 268)	0.806	−0.246
TBA	5.3 (3.1, 6.7)	5.4 (3.1, 6.7)	5.2 (2.6, 7.0)	0.921	−0.099
LDH	230 (186, 292)	228 (184, 281)	256 (187, 373)	0.212	−1.247
HBDH	152.4 (118.9, 179.5)	160.5 (160.5, 160.5)	160.5 (160.5, 165.3)	0.485	−0.698
CK	82.8 (60.5, 107.6)	86.6 (62.2, 109.2)	64.7 (56.8, 100.10)	0.251	−1.148
MYO	20.58 (16.28, 27.94)	20.40 (16.50, 27.58)	21.94 (14.54, 61.50)	0.398	−0.846
CTnT	0.01 (0.01, 0.02)	0.01 (0.00, 0.01)	0.01 (0.00, 0.01)	0.521	−0.641
CK-MB	2.13 (0.41, 5.82)	2.18 (0.41, 5.90)	1.15 (0.10, 3.64)	0.127	−1.526
D-Dimer	0.63 (0.55, 0.63)	190.0 (0.63, 420.0)	135.0 (0.49, 610.0)	0.846	−0.194
BUN	3.5 (2.9, 4.4)	3.5 (3.0, 4.3)	3.5 (2.9, 5.6)	0.62	−0.496
CR	57.8 (49.1, 68.9)	57.2 (48.4, 67.9)	66.4 (52.0, 86.9)	0.126	−1.531
UA	254.5 (209.0, 335.9)	267.8 (214.1, 333.5)	236.5 (180.5, 381.6)	0.795	−0.26
GLU	6.7 (5.6, 7.9)	6.7 (5.4, 7.8)	6.6 (6.0, 8.6)	0.839	−0.203
CA	2.16 (2.03, 2.33)	2.20 (2.06, 2.34)	2.03 (1.97, 2.23)	0.046	−1.994
MG	0.905 (0.843, 0.947)	0.901 (0.843, 0.954)	0.914 (0.742, 0.944)	0.917	−0.104
P	1.00 (0.84, 1.12)	1.00 (0.84, 1.13)	0.99 (0.86, 1.07)	0.567	−0.572
FE	16.9 (13.3, 20.8)	17.3 (14.0, 21.5)	13.4 (7.1, 16.9)	0.004	−2.849
K	4.05 (3.80, 4.35)	4.06 (3.81, 4.37)	3.88 (3.64, 4.25)	0.267	−1.11
NA	140.8 (139.0, 142.9)	140.8 (139.3, 143.2)	139.5 (134.1, 142.2)	0.061	−1.871
CL	101.2 (98.4, 104.9)	101.1 (98.5, 104.8)	101.3 (98.2, 105.6)	0.817	−0.232
IGG	13.03 (11.47, 14.20)	13.01 (11.47, 14.12)	13.87 (11.27, 14.86)	0.481	−0.704
IGA	2.14 (1.64, 2.66)	2.14 (1.62, 2.67)	2.18 (1.69, 2.48)	0.62	−0.495
Continued					

Variable	All (408)	Mild and common group (348)	Severe and critical group (60)	P	Z
IGM	1.22 (0.61, 1.58)	1.22 (0.56, 1.55)	1.21 (0.87, 2.39)	0.219	−1.228
CHOE	9397 (8559, 10,214)	9526 (8752, 10,503)	8955 (7606, 9240)	0.01	−2.584
NT-proBNP	50 (50, 50)	50 (20, 50)	50 (50, 442)	0.008	−2.651
Lopinavir / ritonavir	133 (32.59)	110 (31.61)	23 (38.33)	0.568	0.356
Abidor	141 (34.56)	124 (35.63)	17 (28.33)	0.663	0.178
Combination of two	134 (32.84)	114 (32.76)	20 (33.33)	0.770	0.193

Table 2. Basic characteristics of COVID-19 in mild or common group and severe or critical group in training set. WBC, white blood cell (×109/L); N, neutrophils (×109/L); L, lymphocyte (×109/L); RBC, red blood cell (×1012/L); HB, hemoglobin (g/L); BPC, blood platelet (×109); CRP, C-reactive protein(mg/L); PCT, procalcitonin (ug/L); LA, lactic acid (mmol/L); ESR, erythrocyte sedimentation rate (mm/h); PT, prothrombin time; INR, international standardized ratio; APTT, partial prothrombin time; TT, thrombin time; FIB, Fibrinogen (g/L); FDP, Fibrinogen degradation products (mg/L); TB, total bilirubin (umol/l); ALT, alanine aminotransferase (U/L); AST, aspartate aminotransferase (U/L); GGT, glutamyl transpeptidase (U/L); ALP, alkaline phosphatase (U/L); ALB, albumin (g/L); GLO, globulin (g/L); PALB, prealbumin (g/L); TBA, total bile acid (umol/L); LDH, lactate dehydrogenase (U/L); HBDH, α-hydroxybutyrate dehydrogenase (U/L); CK, creatine kinase (U/L); MYO, myoglobin; CTnT, troponin (ng/ml) ; CK-MB, creatine kinase isoenzyme; BUN, urea nitrogen (mmol/L); CR, creatinine (umol/L); UA, uric acid (umol/L); GLU, blood glucose (mmol/L); CA, calcium (mmol/L); MG, magnesium (mmol/L); P, phosphorus (mmol/L); FE, iron (umol/L); K, potassium (mmol/L); NA, sodium (mmol/L); CL, chlorine (nnol/L); IGG, immunoglobulin G (g/L); IGA, immunoglobulin A(g/L) ; IGM, immunoglobulin M (g/L); CHOE, cholinesterase (U/L).

				95% of EXP(B)C.I						95% of EXP(B) C.I		
	B	S.E	Exp (B)	Low limit	Upper limit	P	B	S.E	Exp(B)	Low limit	Upper limit	P
L	−1.182	0.685	0.307	0.08	1.175	0.085						
LA	0.683	0.506	1.981	0.734	5.343	0.177	7.001	3.437	1097.98	1.304	924,798.262	0.042
ALB	−0.143	0.052	0.866	0.782	0.959	0.006						
CA	−1.425	1.034	0.241	0.032	1.827	0.168						
FE	−0.137	0.049	0.872	0.792	0.961	0.006						
$CD4^+$	−0.029	0.009	0.972	0.955	0.989	0.001						
$CD8^+$	−0.044	0.014	0.957	0.931	0.984	0.002	−0.102	0.04	0.903	0.836	0.976	0.01

Table 4. Univariate and multivariate analysis of the transition from light or ordinary to heavy or critical in training set.

DETECTION OF THE SARS-COV-2 SPIKE PROTEIN IN SALIVA WITH SHRINKY-DINK© ELECTRODES

Zakashansky JA, Imamura AH, Salgado DF 2nd, Romero Mercieca HC, Aguas RFL, Lao AM, Pariser J, Arroyo-Currás N, Khine M.. Anal Methods. 2021 Feb 25;13(7):874-883. doi: 10.1039/d1ay00041a.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

American and Brazilian biotechnology experts collaborate on this proof of mechanism research that demonstrates how the electrodes from a children's toy can be modified to detect SARS-CoV-2 spike protein (S1) in saliva. Researchers utilized an aptamer-based electrochemical assay made from wrinkled electrodes in the Shrinky-Dink toy (See Figure 1) designed to bind specifically to the receptor binding domain of SARS-CoV-2 spike protein, finding this was efficacious for detection of S1 in saliva (See Figure 2, 3). Further studies are needed to validate at different probe densities and to identify the whole virus instead of just S1. These findings suggest potential to increase accessibility of SARS-CoV-2 detection with low-cost screening materials and expansion for wide-range detection and analyses for future epidemics.

ABSTRACT

Using the children's toy, Shrinky-Dink , we present an aptamer-based electrochemical (E-AB) assay that recognizes the spike protein of SARS-CoV-2 in saliva for viral infection detection. The low-cost electrodes are implementable at population scale and demonstrate detection down to 1 ag mL-1 of the S1 subunit of the spike protein.

FIGURES

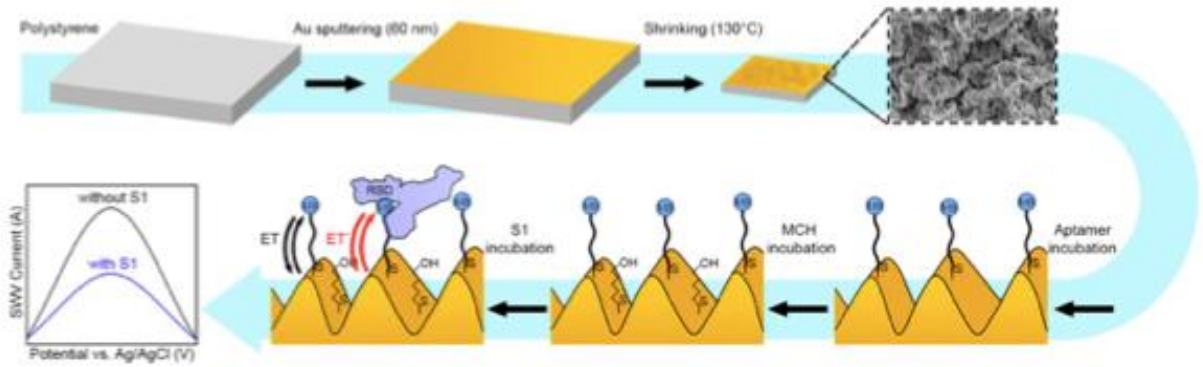

Figure 1. Process flow to create SDW E-AB sensors. First, a thin layer of gold is sputtered onto polystyrene plastic, which is shrunk to create wrinkles (SEM inset shows representative wrinkle morphology). The wrinkled surface is incubated with aptamers conjugated with MB, then incubated with MCH as the blocking molecule. After functionalization, the wrinkled surface was exposed to the S1 protein. Arrows indicate change in electron transfer with and without the spike protein attached (through the RBD). Graph illustrates change in current due to the change in electron transfer for spike bound MB on SDW electrodes upon addition of S1 protein.

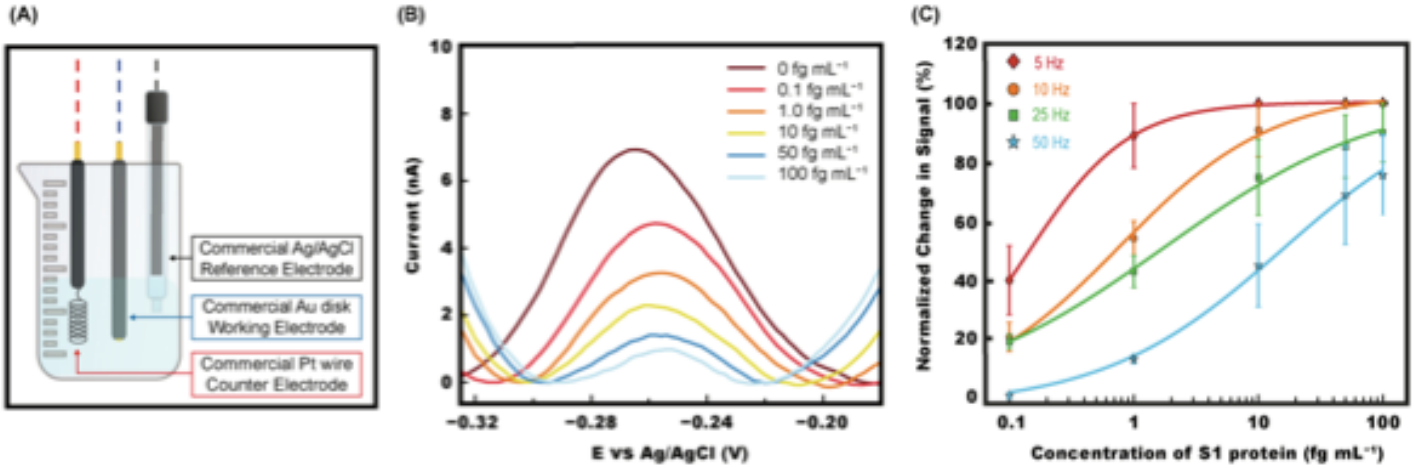

Figure 2. (A) Beaker cell configuration with CD electrode. (B) Raw peak height change in current with increasing concentrations of S1 protein in phosphate buffer solution on CD electrodes. (C) Titration curves collected at various frequencies

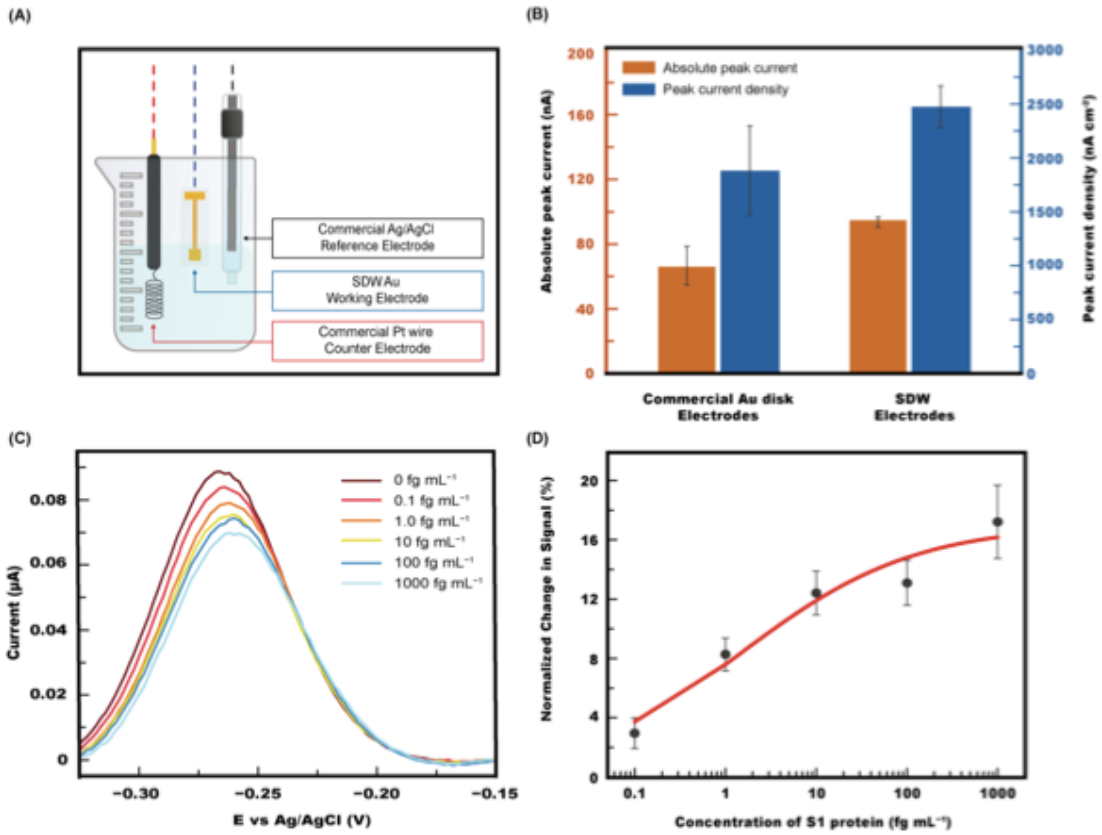

Figure 3. (A) Beaker cell configuration with SWD electrode. (B) Raw peak height change in current with increasing concentrations of S1 protein in 10% saliva on SDW electrodes. (C) Normalized change in signal produced from sequential incubations of saliva spiked with increasing concentrations of S1 protein minus signal from sequentially incubated blank saliva samples. Hill fit represented in red. (D) Methylene blue absolute peak current and peak current density comparison between CD and SDW electrodes with equivalent geometric areas.

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