The Daily COVID-19 Literature Surveillance Summary

April 06, 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

- Transmission of SARS-CoV-2 via fomite, especially cold chain, should not be ignored. In this letter to the editor, authors from the Jilin Provincial Key Laboratory of Animal Embryo Engineering in Changchun, China, review the hardy nature of SARS-CoV-2, stating the virus has an average half-life of 6 hours on plastic and stainless steel, increasing to even longer at colder temperatures (8 hours at 37 °C, 96 hours at 22 °C, and 14 days at 4 °C). This information is especially important when discussing protocols to decrease transmission of SARS-CoV-2 in settings such as live-stock processing plants and cold-chain produce factories. The authors suggest the importance of strict disinfecting, regular testing, and adherence to personal protective equipment to reduce local and global spread of SARS-CoV-2 in these cold-chain settings.

Adjusting Practice During COVID-19

- Time to treatment initiation for breast cancer appear to be unchanged despite the COVID-19 pandemic. A medical student, oncologists, and cancer care experts from the University of Pennsylvania compared a cohort of patients recently diagnosed with early-stage breast cancer between January 1 and May 15, 2018 (pre-COVID-19; n=202) to a cohort diagnosed between January 1 and May 15, 2020 (COVID-19; n=164). In 2020, fewer diagnoses were made (18.8% decrease) and use of preoperative systemic therapy increased (43.9 vs 16.4%; $p<0.001$), but there was no difference in time to treatment initiation after diagnosis ($p=0.926$). Authors believe breast cancer patients diagnosed during the pandemic appear to have received timely care when diagnosed, but the decrease in the number of diagnoses suggests the pandemic may have presented other barriers to care.

- What are considerations regarding the timing of elective surgery and COVID-19 now? Anesthesiologists and surgeons in the United Kingdom detail a consensus statement with recommendations to decrease peri-operative COVID-19 complications in both patients and staff. Their recommendations include: shared decision making between patient and care team, halting planned surgeries of infectious patients, limiting surgery of previously infected patients as long as possible given increased risk of mortality with surgery prior to 7 weeks after recovery, involving multidisciplinary care pre and post-surgery, vaccination if available several weeks before surgery, and strict isolation precautions of COVID-19 positive patients should continue within the hospitals. If postponing the surgery of a previously infected COVID-19 patient is a viable option, this may be very beneficial, given the odds ratio (CI 95%) of 30-day mortality is 4.22 when operating 0-6 weeks post infection vs. 1.02 when waiting until at least 7 weeks. This study suggests that as the pandemic continues, surgical prioritization needs to be taken into account in each case to weigh the risks vs. benefits of surgery in that specific patient, as well as the risk of exposure and transmission to all staff involved.

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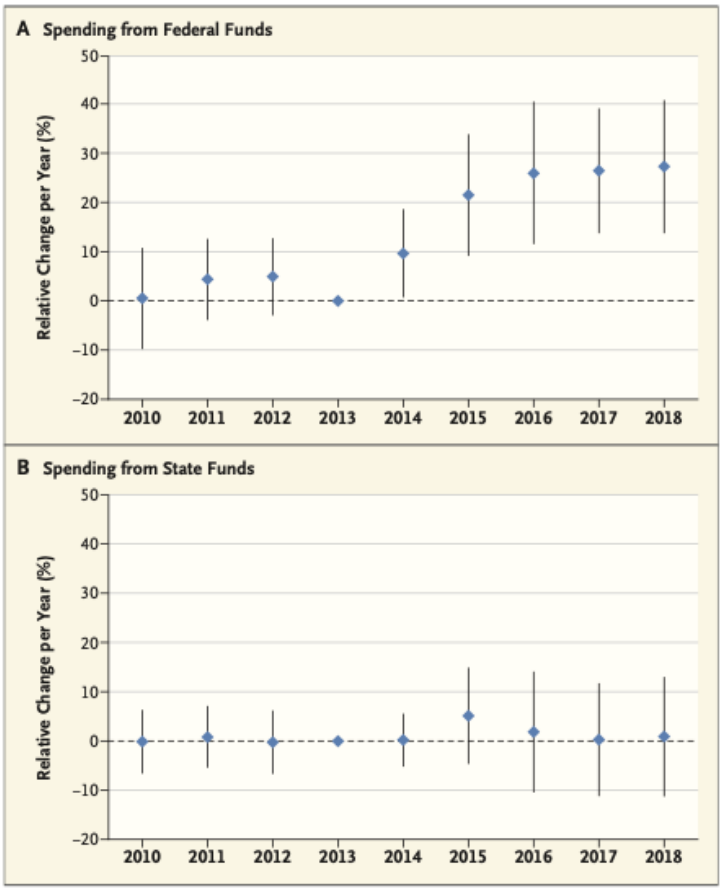
PAYING FOR MEDICAID - STATE BUDGETS AND THE CASE FOR EXPANSION IN THE TIME OF CORONAVIRUS

Gruber J, Sommers BD.. N Engl J Med. 2020 Jun 11;382(24):2280-2282. doi: 10.1056/NEJMp2007124. Epub 2020 Mar 31.
Level of Evidence: 5 - Expert Opinion

BLUF

A perspective article written by researchers associated with Massachusetts Institute of Technology, Harvard Medical School, and Brigham and Women's Hospital discuss how Medicaid expansion states showed 24% higher growth in Medicaid spending compared to 14 non-expansion states, but the increase was entirely subsidized by federal funding (See Graphs), producing a win-win scenario in which millions of low-income adults receive healthcare and safety-net hospitals receive financial support with no adverse effects on state budgets. Recent proposals suggest a cap involving fixed federal Medicaid contributions, however given the recent unexpected cost growth with concurrence of COVID-19 crisis, public health disaster, and ongoing opioid epidemic, it is suggested that now is a perfect time to bolster the Medicaid system with further Medicaid expansion to increase health care resources and infuse federal dollars into state economies, especially given no requirement for new infrastructure or federal oversight.

FIGURES



Changes in State Spending Associated with Medicaid Expansion, Using Federal Funds as Compared with State Funds, 2010–2018.
The graphs show changes per year for states that have expanded Medicaid as of 2018, as compared with nonexpansion states, with 2013 as the reference year. Bars show 95% confidence intervals, using robust state-clustered standard errors. Models adjust for state-year unemployment rates and per capita income. Adapted from Gruber and Sommers.3

ADULTS

COVID-19 AND GENDER: LOWER RATE BUT SAME MORTALITY OF SEVERE DISEASE IN WOMEN-AN OBSERVATIONAL STUDY

Raimondi F, Novelli L, Ghirardi A, Russo FM, Pellegrini D, Biza R, Trapasso R, Giuliani L, Anelli M, Amoroso M, Allegri C, Imeri G, Sanfilippo C, Comandini S, Hila E, Manesso L, Gandini L, Mandelli P, Monti M, Gori M, Senni M, Lorini FL, Rizzi M, Barbui T, Paris L, Rambaldi A, Cosentini R, Guagliumi G, Cesa S, Colledan M, Sessa M, Masciulli A, Gavazzi A, Buoro S, Remuzzi G, Ruggenenti P, Callegaro A, Gianatti A, Farina C, Bellasi A, Sironi S, Fagiuoli S, Di Marco F; HPG23 Covid-19 Study Group.. BMC Pulm Med. 2021 Mar 20;21(1):96. doi: 10.1186/s12890-021-01455-0.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

Investigators from various academic and medical institutions in Bergamo, Italy conducted a retrospective observational study of 431 COVID-19 patients admitted to Papa Giovanni XXIII Hospital and San Giovanni Bianco Hospital between February 23 - March 14, 2020 analyzing the relationship between gender, clinical features, and 28-day outcomes. They found a lower prevalence in women with only 27.6% of admissions (p = 0.54), as well as lower rates of 28-day mortality (p = 0.018) and severe disease in women (p = 0.898); once severe disease occurred, however, the risk of dying was not affected by gender (Figure 2). The authors suggest further research to better characterize specific sex and gender-related parameters, allowing for more individualized care for COVID-19 patients.

ABSTRACT

BACKGROUND: Gender-related factors might affect vulnerability to Covid-19. The aim of this study was to describe the role of gender on clinical features and 28-day mortality in Covid-19 patients. METHODS: Observational study of Covid-19 patients hospitalized in Bergamo, Italy, during the first three weeks of the outbreak. Medical records, clinical, radiological and laboratory findings upon admission and treatment have been collected. Primary outcome was 28-day mortality since hospitalization. RESULTS: 431 consecutive adult patients were admitted. Female patients were 119 (27.6%) with a mean age of 67.0 +- 14.5 years (vs 67.8 +- 12.5 for males, p = 0.54). Previous history of myocardial infarction, vasculopathy and former smoking habits were more common for males. At the time of admission PaO2/FiO2 was similar between men and women (228 [IQR, 134-273] vs 238 mmHg [150-281], p = 0.28). Continuous Positive Airway Pressure (CPAP) assistance was needed in the first 24 h more frequently in male patients (25.7% vs 13.0%; p = 0.006). Overall 28-day mortality was 26.1% in women and 38.1% in men (p = 0.018). Gender did not result an independent predictor of death once the parameters related to disease severity at presentation were included in the multivariable analysis (p = 0.898). Accordingly, the Kaplan-Meier survival analysis in female and male patients requiring CPAP or non-invasive ventilation in the first 24 h did not find a significant difference (p = 0.687). CONCLUSION: Hospitalized women are less likely to die from Covid-19; however, once severe disease occurs, the risk of dying is similar to men. Further studies are needed to better investigate the role of gender in clinical course and outcome of Covid-19.

FIGURES

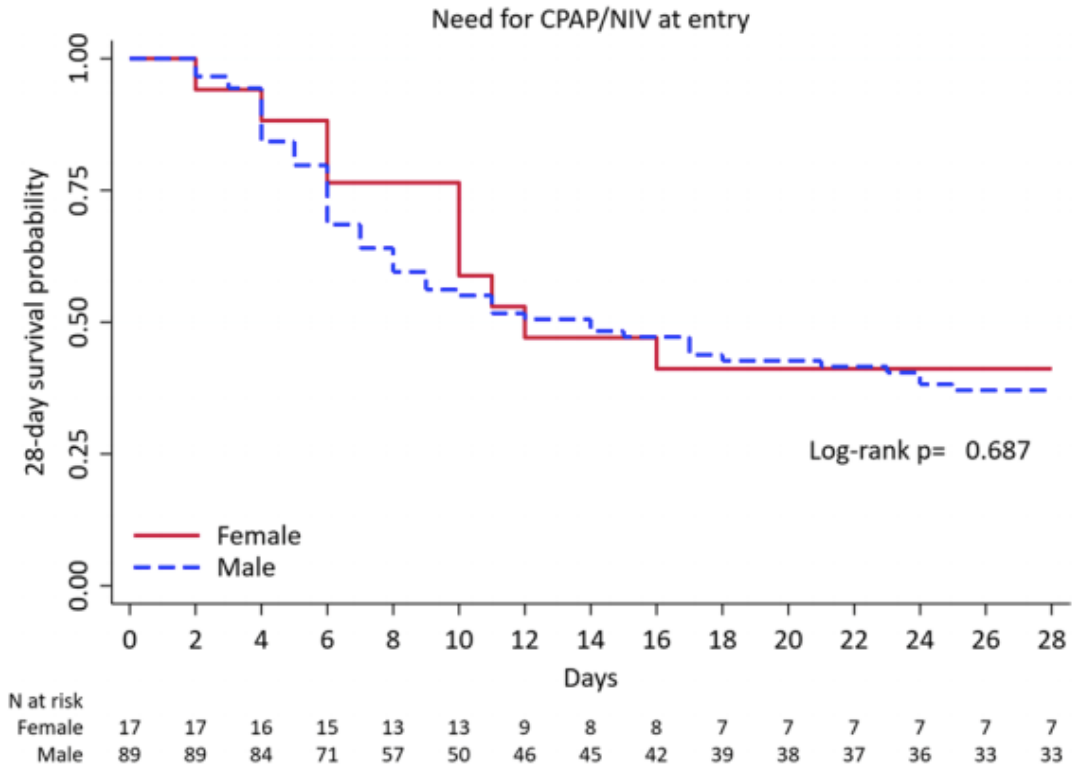


Figure 2. Kaplan–Meier 28-day mortality since hospitalization by gender in patients who needed CPAP/NIV in the first 24 h. CPAP Continuous positive airway pressure, NIV non-invasive ventilation.

TRANSMISSION OF SARS-COV-2 VIA FOMITE, ESPECIALLY COLD CHAIN, SHOULD NOT BE IGNORED

Ji W, Li X, Chen S, Ren L.. Proc Natl Acad Sci U S A. 2021 Mar 16;118(11):e2026093118. doi: 10.1073/pnas.2026093118.
Level of Evidence: 5 - Review / Literature Review

BLUF

In this letter to the editor, authors from the Jilin Provincial Key Laboratory of Animal Embryo Engineering in Changchun, China, review the hardy nature of SARS-CoV-2, stating the virus has an average half-life of 6 hours on plastic and stainless steel, increasing to even longer at colder temperatures (8 hours at 37 °C, 96 hours at 22 °C, and 14 days at 4 °C). This information is especially important when discussing protocols to decrease transmission of SARS-CoV-2 in settings such as live-stock processing plants and cold-chain produce factories. The authors suggest the importance of strict disinfecting, regular testing, and adherence to personal protective equipment to reduce local and global spread of SARS-CoV-2 in these cold-chain settings.

HEMATOLOGY AND ONCOLOGY

TIME TO TREATMENT INITIATION FOR BREAST CANCER DURING THE 2020 COVID-19 PANDEMIC

Hawrot K, Shulman LN, Bleiweiss IJ, Wilkie EJ, Frosch ZAK, Jankowitz RC, Laughlin AI.. JCO Oncol Pract. 2021 Mar 12:OP2000807. doi: 10.1200/OP.20.00807. Online ahead of print.
Level of Evidence: 4 - Local non-random sample

BLUF

A medical student, oncologists, and cancer care experts from the University of Pennsylvania compared a cohort of patients recently diagnosed with early-stage breast cancer between January 1 and May 15, 2018 (pre-COVID-19; n=202) to a cohort diagnosed between January 1 and May 15, 2020 (COVID-19; n=164)(Table 1). In 2020, fewer diagnoses were made (18.8% decrease) and use of preoperative systemic therapy increased (43.9 vs 16.4%; p<0.001), but there was no difference in time to treatment initiation after diagnosis (p=0.926)(Tables 2, 3). Authors believe breast cancer patients diagnosed during the pandemic appear to have received timely care when diagnosed, but the decrease in the number of diagnoses suggests the pandemic may have presented other barriers to care.

ABSTRACT

PURPOSE: The COVID-19 pandemic has posed significant pressures on healthcare systems, raising concern that related care delays will result in excess cancer-related deaths. Because data regarding the impact on patients with breast cancer are urgently needed, we aimed to provide a preliminary estimate of the impact of COVID-19 on time to treatment initiation (TTI) for patients newly diagnosed with breast cancer cared for at a large academic center. METHODS: We conducted a retrospective study of patients with newly diagnosed early-stage breast cancer between January 1, 2020, and May 15, 2020, a time period during which care was affected by COVID-19, and an unaffected cohort diagnosed between January 1, 2018 and May 15, 2018. Outcomes included patient volume, TTI, and initial treatment modality. Adjusted TTI was compared using multivariable linear regression. RESULTS: Three hundred sixty-six patients were included. There was an 18.8% decrease in patient volume in 2020 (n = 164) versus 2018 (n = 202). There was no association between time of diagnosis (pre-COVID-19 or during COVID-19) and adjusted TTI (P = .926). There were fewer in situ diagnoses in the 2020 cohort (P = .040). There was increased use of preoperative systemic therapy in 2020 (43.9% overall, 20.7% chemotherapy, and 23.2% hormonal therapy) versus 2018 (16.4% overall, 12.4% chemotherapy, and 4.0% hormonal therapy) (P < .001). CONCLUSION: TTI was maintained among patients diagnosed and treated for breast cancer during the COVID-19 pandemic at a single large academic center. There was a decrease in patient volume, specifically in patients with in situ disease and a shift in initial therapy toward the use of preoperative hormonal therapy.

FIGURES

TABLE 1. Patient Characteristics

Characteristic	2018 n = 202		2020 n = 164		P
	n	%	n	%	
Age, years					.307
< 50	63	31.2	42	25.6	
50-70	96	47.5	91	55.5	
> 70	43	21.3	31	18.9	
Race					.217
White	136	67.7	104	63.4	
Black	54	26.5	42	25.6	
Others	12	5.8	18	11.0	
Clinical stage at presentation					.040
0	53	26.2	22	13.4	
I	102	50.5	93	56.7	
II	33	16.3	35	21.3	
III	10	5.0	12	7.3	
Unknown or not applicable	4	2.0	2	1.2	
Type of initial therapy					< .001
Definitive surgery	167	82.7	87	53.1	
Neoadjuvant chemotherapy	25	12.4	34	20.7	
Radiation	2	1.0	0	3.1	
Preoperative hormonal therapy	8	4.0	38	23.2	
Breast cancer subtype (invasive cancer only)	n = 149		n = 142		.941
HR-positive	99	66.4	99	69.7	
HER2-positive	24	16.1	21	14.8	
TNBC	24	16.1	20	14.1	
Unknown or not applicable	2	1.3	2	1.4	
Histology (invasive cancer only)	n = 149		n = 142		.062
Invasive ductal	110	73.8	115	81.0	
Invasive lobular	18	12.1	18	12.7	
Invasive mixed	9	6	7	4.9	
Others	12	8.1	2	1.4	

NOTE. Clinical stage based on American Joint Committee on Cancer Cancer Staging Manual, Eighth Edition (2017).
Abbreviations: HER2, human epidermal growth factor receptor 2; HR, hormone receptor; TNBC, triple-negative breast cancer.

Table 1. Patient Characteristics.

TABLE 2. Adjusted TTI by Cohort

Cohort	TTI[a] (days)	95% CI	P
2018	44.7	41.2 to 48.2	.926
2020	44.4	40.5 to 48.4	

Abbreviation: TTI, time to treatment initiation.

[a]Reported at means of covariates: race, age group, clinical stage, breast cancer subtype, and histologic subtype.

TABLE 3. Exploratory Outcomes in the 2020 Cohort

Characteristic	2020		
	Mean	Median	IQR
Time, days (n = 164)			
Time from presentation to histologic diagnosis	38	23	13-48
Time from histologic diagnosis to initial appointment	17	14	8-21
Time from initial appointment to treatment	27	22	15-33
Time from histologic diagnosis to treatment	44	36	27-52
Type of initial presentation (n = 103)		n	%
Screening mammogram		54	52.4
Self-palpated mass		43	41.8
Others		6	5.8
Type of delay (n = 99)			
No care delay		55	55.6
Care delay identified		44	44.4
Surgery		41	
Radiation therapy		27	
Chemotherapy		4	
Type of initial therapy (n = 164)			
Breast conserving surgery		57	34.8
Neoadjuvant hormonal therapy		38	23.2
Neoadjuvant chemotherapy		21	12.8
Mastectomy without reconstruction		13	7.9
Neoadjuvant chemotherapy with HER2-targeted therapy		13	7.9
Mastectomy with tissue-based reconstruction		9	5.5
Mastectomy with implant-based reconstruction		8	4.9
Patient declined therapy		5	3.1

Abbreviation: HER2, human epidermal growth factor receptor 2.

SARS-COV-2 INFECTION, COVID-19 AND TIMING OF ELECTIVE SURGERY: A MULTIDISCIPLINARY CONSENSUS STATEMENT ON BEHALF OF THE ASSOCIATION OF ANAESTHETISTS, THE CENTRE FOR PERI-OPERATIVE CARE, THE FEDERATION OF SURGICAL SPECIALTY ASSOCIATIONS, THE ROYAL COLLEGE OF ANAESTHETISTS AND THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

El-Boghdadly K, Cook TM, Goodacre T, Kua J, Blake L, Denmark S, McNally S, Mercer N, Moonesinghe SR, Summerton DJ.. Anaesthesia. 2021 Mar 18. doi: 10.1111/anae.15464. Online ahead of print.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

Anesthesiologists and surgeons in the United Kingdom detail a consensus statement with recommendations to decrease peri-operative COVID-19 complications in both patients and staff. Their recommendations include: shared decision making between patient and care team, halting planned surgeries of infectious patients, limiting surgery of previously infected patients as long as possible given increased risk of mortality with surgery prior to 7 weeks after recovery, involving multidisciplinary care pre and post-surgery, vaccination if available several weeks before surgery, and strict isolation precautions of COVID-19 positive patients should continue within the hospitals. If postponing the surgery of a previously infected COVID-19 patient is a viable option, this may be very beneficial, given the odds ratio (CI 95%) of 30-day mortality is 4.22 when operating 0-6 weeks post infection vs. 1.02 when waiting until at least 7 weeks. This study suggests that as the pandemic continues, surgical prioritization (Box 1) needs to be taken into account in each case to weigh the risks vs. benefits of surgery in that specific patient, as well as the risk of exposure and transmission to all staff involved.

ABSTRACT

The scale of the COVID-19 pandemic means that a significant number of patients who have previously been infected with SARS-CoV-2 will require surgery. Given the potential for multisystem involvement, timing of surgery needs to be carefully considered to plan for safe surgery. This consensus statement uses evidence from a systematic review and expert opinion to highlight key principles in the timing of surgery. Shared decision-making regarding timing of surgery after SARS-CoV-2 infection must account for severity of the initial infection; ongoing symptoms of COVID-19; comorbid and functional status; clinical priority and risk of disease progression; and complexity of surgery. For the protection of staff, other patients and the public, planned surgery should not be considered during the period that a patient may be infectious. Precautions should be undertaken to prevent pre- and peri-operative infection, especially in higher risk patients. Elective surgery should not be scheduled within 7 weeks of a diagnosis of SARS-CoV-2 infection unless the risks of deferring surgery outweigh the risk of postoperative morbidity or mortality associated with COVID-19. SARS-CoV-2 causes either transient or asymptomatic disease for most patients, who require no additional precautions beyond a 7-week delay, but those who have persistent symptoms or have been hospitalised require special attention. Patients with persistent symptoms of COVID-19 are at increased risk of postoperative morbidity and mortality even after 7 weeks. The time before surgery should be used for functional assessment, prehabilitation and multidisciplinary optimisation. Vaccination several weeks before surgery will reduce risk to patients and might lessen the risk of nosocomial SARS-CoV-2 infection of other patients and staff. National vaccine committees should consider whether such patients can be prioritised for vaccination. As further data emerge, these recommendations may need to be revised, but the principles presented should be considered to ensure safety of patients, the public and staff.

FIGURES

Box 1

Prioritisation of urgency of surgical procedures [6]. Categories P5 (patient wishes to postpone surgery due to COVID-19 concerns) and P6 (patient wishes to postpone surgery due to non-COVID-19 concerns) were added in October 2020 as part of the national validation of waiting lists [40].

Priority 1a: Emergency procedures to be performed in < 24 h.

Priority 1b: Procedures to be performed in < 72 h

Priority 2: Procedures to be performed in < 1 month

Priority 3: Procedures to be performed in < 3 months

Priority 4: Procedures to be performed in > 3 months

Box 1

IMMUNO-INFORMATICS DESIGN OF A MULTIMERIC EPITOPE PEPTIDE BASED VACCINE TARGETING SARS-COV-2 SPIKE GLYCOPROTEIN

Chukwudozie OS, Gray CM, Fagbayi TA, Chukwuanukwu RC, Oyebanji VO, Bankole TT, Adewole RA, Daniel EM.. PLoS One. 2021 Mar 17;16(3):e0248061. doi: 10.1371/journal.pone.0248061. eCollection 2021.
Level of Evidence: 5 - Modeling

BLUF

Investigators from various academic and medical institutions in Nigeria and South Africa conducted a promising in silico design of a model vaccine with epitope candidates against SARS-CoV-2 spike glycoprotein including 27 B cell epitopes, 8 CD8+ T cell epitopes, and 12 CD4+ T cell epitopes, covalently linked with an immuno-adjuvant (Figure 4). They then used a Java Codon Adaptation Tool (JCat) to increase the translational vaccine rate in E. coli, as well as simulation of stimulated immune cells in different anatomical sites of primary and secondary lymphoid organs. The results revealed high antigen detection and cell mediated immunity (Figure 8), suggesting epitope-based vaccines as possible longterm options to fight COVID-19 with a yearly injection.

ABSTRACT

Developing an efficacious vaccine for SARS-CoV-2 infection is critical to stemming COVID-19 fatalities and providing the global community with immune protection. We have used a bioinformatic approach to aid in designing an epitope peptide-based vaccine against the spike protein of the virus. Five antigenic B cell epitopes with viable antigenicity and a total of 27 discontinuous B cell epitopes were mapped out structurally in the spike protein for antibody recognition. We identified eight CD8+ T cell 9-mers and 12 CD4+ T cell 14-15-mer as promising candidate epitopes putatively restricted by a large number of MHC I and II alleles, respectively. We used this information to construct an in silico chimeric peptide vaccine whose translational rate was highly expressed when cloned in pET28a (+) vector. With our In silico test, the vaccine construct was predicted to elicit high antigenicity and cell-mediated immunity when given as a homologous prime-boost, triggering of toll-like receptor 5 by the adjuvant linker. The vaccine was also characterized by an increase in IgM and IgG and an array of Th1 and Th2 cytokines. Upon in silico challenge with SARS-CoV-2, there was a decrease in antigen levels using our immune simulations. We, therefore, propose that potential vaccine designs consider this approach.

FIGURES

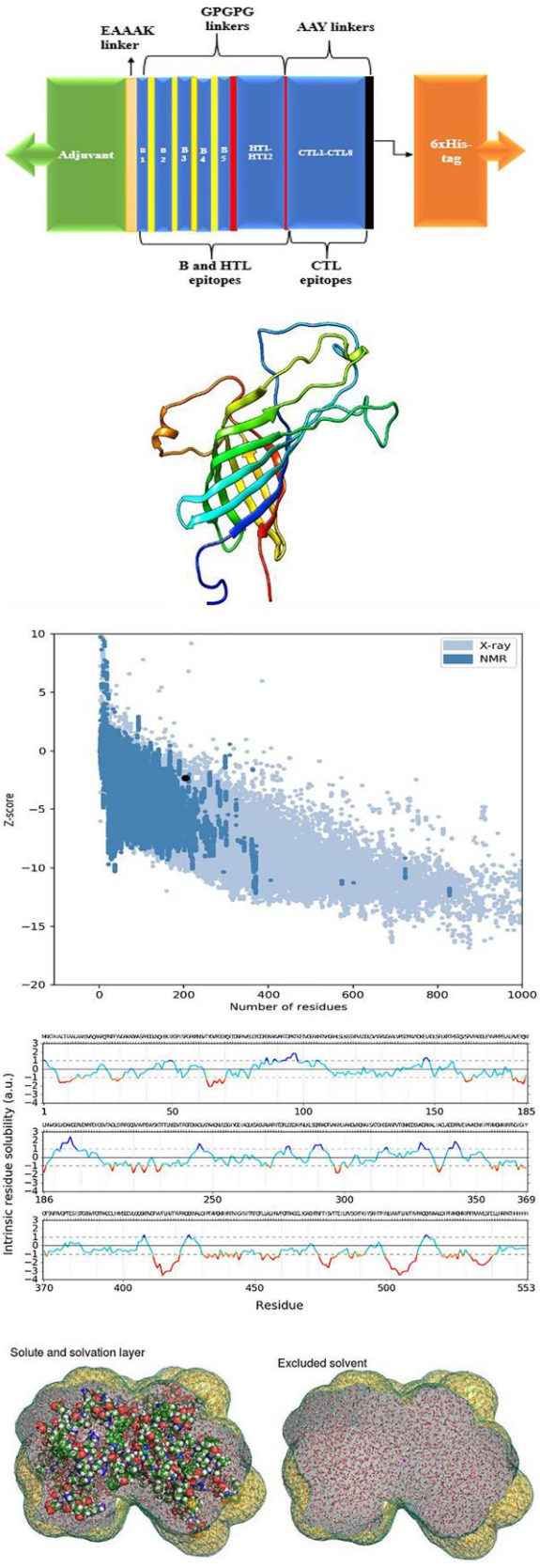


Fig 4. (a) Schematic presentation of the vaccine containing an adjuvant (green) linked with the multi-epitope sequence through an EAAAK linker. The B and HTL epitopes are linked together via the GPGPG linkers while the CTL epitopes are linked with the help of AAY linkers. The 6x-His tag at the carboxyl end. (b) Tertiary structure of the vaccine. (c) Validation of the structure with a Z score of −2.32. (d) Intrinsic solubility profile. Residues lesser than -1 depicts the hydrophobic core of the vaccine peptide. (e) The solute and solvation layer of the vaccine

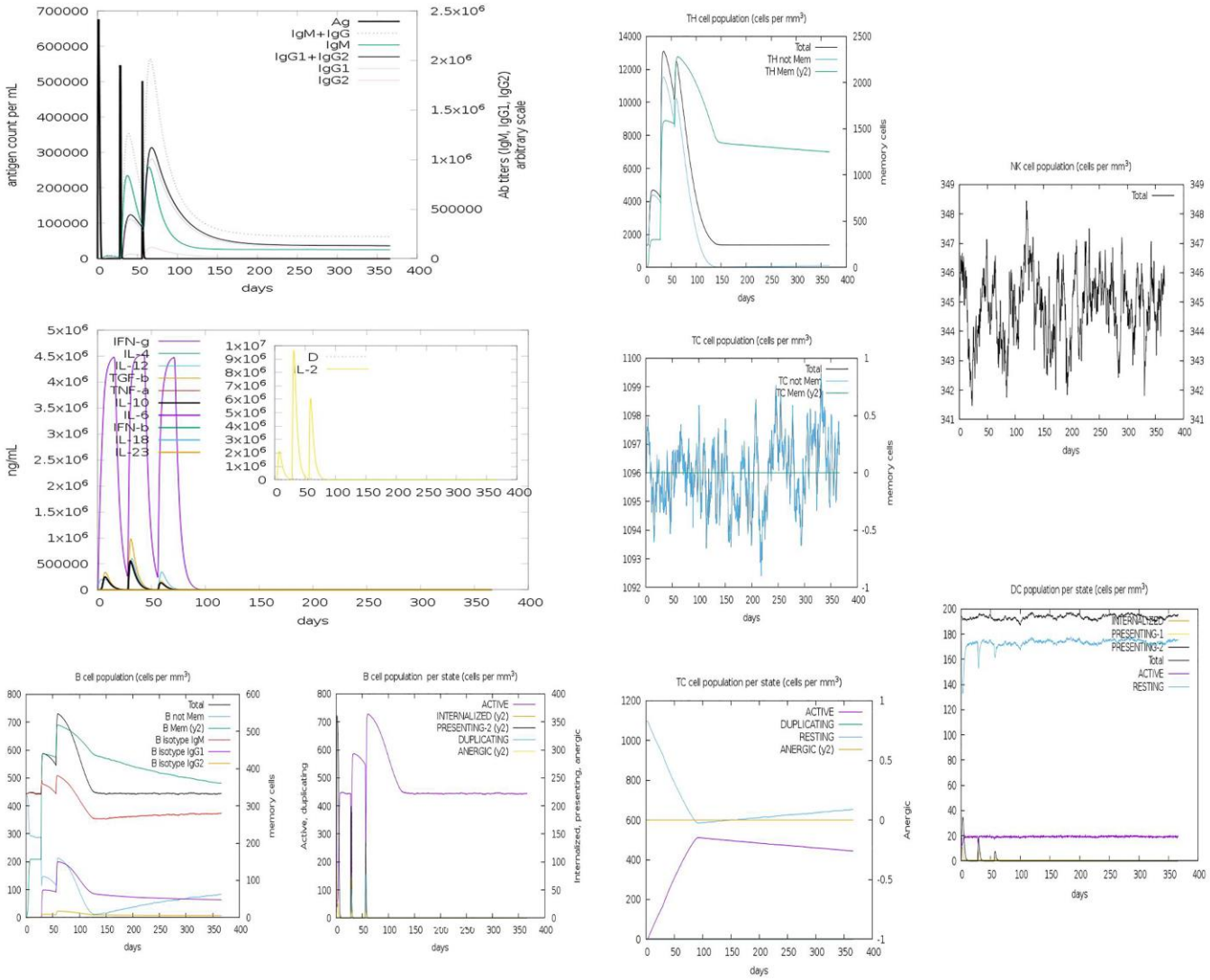


Fig 8. The induced immune cells by the peptide vaccines. (a) The concomitant decrease in antigen level with rise in immunoglobin activities. (b) Induced array of cytokines during prime boost. (c) B lymphocytes: total count, memory cells, and sub-divided in isotypes IgM, IgG1 and IgG2. (d) CD4 T-helper lymphocytes count. (e) CD4 T-helper lymphocytes count. (f) CD8 T-cytotoxic lymphocytes count. (g) CD8 T-cytotoxic lymphocytes count per entity-state. (h) Natural Killer cells (total count). (i) Dendritic cells.

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CONTRIBUTORS

Hamza Sultan
Renate Meckl
Veronica Graham

EDITORS

John Michael Sherman
Julia Ghering
Maresa Woodfield

SENIOR EDITORS

Allison Hansen
Avery Forrow

SENIOR EXECUTIVE EDITOR

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