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# Hawai‘i Journal of Health & Social Welfare

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**Aim:**
The aim of the Hawai‘i Journal of Health & Social Welfare is to advance knowledge about health and social welfare, with a focus on the diverse peoples and unique environments of Hawai‘i and the Pacific region.

**History:**
In 1941, a journal then called The Hawai‘i Medical Journal was founded by the Hawai‘i Medical Association (HMA). The HMA had been incorporated in 1856 under the Hawaiian monarchy. In 2008, a separate journal called the Hawai‘i Journal of Public Health was established by a collaborative effort between the Hawai‘i State Department of Health and the University of Hawai‘i at Mānoa Office of Public Health Studies. In 2012, these two journals merged to form the Hawai‘i Journal of Medicine & Public Health, and this journal continued to be supported by the Hawai‘i State Department of Health and the John A. Burns School of Medicine.

In 2018, the number of partners providing financial backing for the journal expanded, and to reflect this expansion the name of the journal was changed in 2019 to the Hawai‘i Journal of Health & Social Welfare. The lead academic partners are now the six units of the UH College of Health Sciences and Social Welfare, including the John A. Burns School of Medicine, UH Public Health, the Thompson School of Social Work & Public Health, the School of Nursing and Dental Hygiene, the UH Cancer Center, and the Daniel K. Inouye College of Pharmacy. Other partners are the Hawai‘i State Department of Health and the UH Office of the Vice Chancellor for Research. The journal is fiscally managed by University Health Partners of Hawai‘i.

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# Hawai'i Journal Watch

Karen Rowan MS

***Highlights of recent research from the University of Hawai'i and the Hawai'i State Department of Health***

## Common Cardiac Arrhythmia Among Older Japanese Men in Hawai'i Shows Paradoxical Relationship

High cholesterol levels are a risk factor for heart disease. However, older Japanese men in Hawai'i may present an example of the "dyslipidemia paradox" because those with higher cholesterol show a lower rate of atrial fibrillation/atrial flutter (AF), a common cardiac arrhythmia. Researchers including Tagayasu Anzai MD, PhD, of the Thompson School of Social Work & Public Health, conducted a cross-sectional analysis of cholesterol levels in 3741 participants in their 70s and 80s in the ongoing Kuakini Honolulu Heart Program. Results showed that 4.5% of participants had AF, but among participants older than 75, those whose levels of low-density lipoprotein cholesterol (LDL) or total cholesterol were in the lowest quartile of all participants had higher rates of AF than those with higher LDL or total cholesterol levels. More research is needed to better understand the paradox.

- Anzai T, Grandinetti A, Katz AR, Hurwitz EL, Wu YY, Masaki K. Paradoxical association between atrial fibrillation/flutter and high cholesterol over age 75 years: The Kuakini Honolulu Heart Program and Honolulu-Asia Aging Study. *J Electrocardiol*. 2020;65:37-44. doi:10.1016/j.jelectrocard.2020.12.008

## Pharmacy Students in Hawai'i Benefit from Educational Instagram Posts

Instagram posts may help pharmacy students in Hawai'i increase their knowledge of medications. Researchers led by Jarred Prudencio, PharmD, of the Daniel K. Inouye College of Pharmacy, created an Instagram account and invited doctoral pharmacy students who were starting an ambulatory care rotation in a family medicine clinic to follow it. The faculty posted clinical pearls three times weekly during the semester; 32 students choose to follow the account while 37 did not. The students who followed the account improved their scores on a 30-question knowledge test by significantly more than students who did not (15% vs 3.1%). The researchers concluded that social media platforms offer a highly accessible way to improve pharmacy student learning.

- Prudencio J, Wongwiwatthananukit S, Lozano A, Xu Y. Instagram as a tool to enhance pharmacy student learning of ambulatory care pharmacy. *Curr Pharm Teach Learn*. 2021;13(2):134-138. doi:10.1016/j.cptl.2020.09.007

## Cyanobacteria Found in Saliva of Areca Nut Chewers

Chewing areca nuts is common in some parts of the Pacific and has been linked to increased oral cancer risk. New findings show that cyanobacteria and their toxic metabolites are found in the nuts and other parts of the plants, as well as in the saliva of chewers. Researchers led by Brenda Y. Hernandez, PhD, MPH, of the UH Cancer Center, analyzed samples from husks, nuts, and leaves of the *Areca catechu* plant, and leaves of the *Piper betle*, which are sometimes chewed with areca nuts. They also analyzed saliva samples from 122 adults on Guam, including 64 current betel nut chewers, 37 former chewers, and 21 people with no history of betel nut use. Results revealed cyanobacteria DNA in all plant samples and all saliva samples, but at significantly higher levels in the current chewers compared with those who did not chew the nuts. Cyanotoxins were also found in both plant and saliva samples. More research is needed to understand the relationship between cyanobacteria and cancer development.

- Hernandez BY, Zhu X, Sotto P, Paulino Y. Oral exposure to environmental cyanobacteria toxins: Implications for cancer risk. *Environ Int*. 2021;148:106381. doi:10.1016/j.envint.2021.106381

## Health Literacy Among Former Soviet Union Immigrants

International migrants comprise 3.5% of the world's population. Former Soviet Union (FSU) immigrants are the fourth-largest group of migrants in the world, with substantial diasporas in the US, Germany, and Israel. An international multidisciplinary research team led by Uliana Kostareva BSN, RN, of the School of Nursing and Dental Hygiene, conducted an integrative literature review in 4 languages on health literacy of FSU immigrants. Only articles from Israel measured health literacy of FSU immigrants; it was lower than the health literacy of the general population. The majority of articles focused on older FSU immigrants, and all articles stressed the need for translated and culturally relevant health information. Despite clear needs, FSU immigrants are underrepresented in health literacy research. The review provided a model of a comprehensive multilingual search.

- Kostareva U, Albright CL, Berens EM, Polansky P, Kadish DE, Ivanov LL, Sentell TL. A multilingual integrative review of health literacy in Former Soviet Union, Russian-speaking immigrants. *Int J Environ Res Public Health*. 2021;18(2):657. doi:10.3390/ijerph18020657

# Genetic Characteristics and Phylogeny of 969-bp S Gene Sequence of SARS-CoV-2 from Hawai‘i Reveals the Worldwide Emerging P681H Mutation

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## Abstract

*The COVID-19 pandemic has ravaged the world, caused over 1.8 million deaths in its first year, and severely affected the global economy. Hawai‘i has not been spared from the transmission of SARS-CoV-2 in the local population, including high infection rates in racial and ethnic minorities. Early in the pandemic, we described in this journal various technologies used for the detection of SARS-CoV-2. Herein we characterize a 969-bp SARS-CoV-2 segment of the S gene downstream of the receptor-binding domain. At the John A. Burns School of Medicine Biocontainment Facility, RNA was extracted from an oropharyngeal swab and a nasal swab from 2 patients from Hawai‘i who were infected with SARS-CoV-2 in August 2020. Following PCR, the 2 viral strains were sequenced using Sanger sequencing, and phylogenetic trees were generated using MEGAX. Phylogenetic tree results indicate that the virus has been introduced to Hawai‘i from multiple sources. Further, we decoded 13 single nucleotide polymorphisms across 13 unique SARS-CoV-2 genomes within this region of the S gene, with 1 non-synonymous mutation (P681H) found in the 2 Hawai‘i strains. The P681H mutation has unique and emerging characteristics with a significant exponential increase in worldwide frequency when compared to the plateauing of the now universal D614G mutation. The P681H mutation is also characteristic of the new SARS-CoV-2 variants from the United Kingdom and Nigeria. Additionally, several mutations resulting in cysteine residues were detected, potentially resulting in disruption of the disulfide bridges in and around the receptor-binding domain. Targeted sequence characterization is warranted to determine the origin of multiple introductions of SARS-CoV-2 circulating in Hawai‘i.*

## Keywords

*S gene, spike protein, phylogenetic tree, genomic characterization, Hawai‘i strains, single nucleotide polymorphism, variant, proline*

## Abbreviations

*ASGPB = Advanced Studies in Genomics, Proteomics, and Bioinformatics*
*A1708D = alanine to aspartic acid at amino acid 1708*
*A570D = alanine to aspartic acid at amino acid 570*
*A522S = alanine to serine at amino acid 522*
*A771S = alanine to serine at amino acid 771*
*ACE2 = angiotensin-converting enzyme 2*
*R577C = arginine to cysteine at amino acid 577*
*R52I = arginine to isoleucine at amino acid 52*
*N501Y = asparagine to tyrosine at amino acid 501*
*D614G = aspartic acid to glycine at amino acid 614*
*D1118H = aspartic acid to histidine at amino acid 1118*
*D3L = aspartic acid to leucine at amino acid 3*
*cDNA = complementary deoxyribonucleic acid*
*COVID-19 = coronavirus disease 2019*
*ΔG2676 = deletion of glycine amino acid 2676*
*ΔH69 = deletion of histidine amino acid 69*
*ΔF3677 = deletion of phenylalanine amino acid 3677*
*ΔS3675 = deletion of serine amino acid 3675*
*ΔY145 = deletion of tyrosine amino acid 145*
*ΔV70 = deletion of valine amino acid 70*
*DNA = deoxyribonucleic acid*
*EUA = emergency use authorization*
*GISAID = Global Initiative of Sharing All Influenza Data*
*E780Q = glutamic acid to glutamine at amino acid 780*
*Q27stop = glutamine to stop codon at amino acid 27*
*IBC = Institutional Biosafety Committee*
*IRB = Institutional Review Board*
*I726F = isoleucine to phenylalanine at amino acid 726*
*I2230T = isoleucine to threonine at amino acid 2230*
*I584V = isoleucine to valine at amino acid 584*
*MUSCLE = Multiple Sequence Comparison by Log-Expectation*
*NCBI = National Center for Biotechnology Information*
*NERVTAG = New and Emerging Respiratory Virus Threats Advisory Group*
*nCoV = novel coronavirus*
*PID = patient identification*
*F797C = phenylalanine to cysteine at amino acid 797*
*F543L = phenylalanine to leucine at amino acid 543*
*PCR = polymerase chain reaction*
*P681H = proline to histidine at amino acid 681*
*RBD = receptor-binding domain*
*RT-PCR = reverse transcriptase-polymerase chain reaction*
*RNA = ribonucleic acid*
*S982A = serine to alanine at amino acid 982*
*S680C = serine to cysteine at amino acid 680*
*S235F = serine to phenylalanine at amino acid 235*
*SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2*
*SNP = single nucleotide polymorphism*
*T1001I = threonine to isoleucine at amino acid 1001*
*T716I = threonine to isoleucine at amino acid 716*
*TBE = tris/borate/ethylenediaminetetraacetic acid*
*Y73C = tyrosine to cysteine at amino acid 73*
*FDA = Food and Drug Administration*
*VOC = variant of concern*
*VTM = viral transport media*

## Introduction

The zoonotic virus responsible for the present Coronavirus disease 2019 (COVID-19) pandemic is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly novel coronavirus [nCoV]).[1] SARS-CoV-2 emerged in Wuhan, China, at a seafood market in November 2019 and has been evolving ever since.[1-4] The COVID-19 pandemic resultant from SARS-CoV-2 has been responsible for infecting more than 107 million people worldwide and has been fatal in more than 2.3 million persons experiencing an infection.[5] The state of Hawai‘i has reported more than 26 000 cases and 400 deaths, with daily reports steady at approximately 60 new cases per day since August 2020.[6]

To understand SARS-CoV-2 emergence and the disease COVID-19, one must look at the genome as the virus evolves and emerges through genomic alterations and adaptations. SARS-CoV-2 belongs to the family of *Coronaviridae* (genus Betacoronavirus), which are viruses with 26 000–32 000 nucleotide long single-stranded positive-sense RNA genomes.[7–9] Geneticists and virologists look at the SARS-CoV-2 genome and its adaptations to analyze the nucleotide and amino acid variations. Analysis of the SARS-CoV-2 genome will allow us to track the spread through unique genomic fingerprints,[1] determine whether these adaptations alter the viral fitness, infectious capabilities,[10] and develop potential vaccines and therapeutics.[11,12]

While genes encode 20 proteins consisting of 4 structural and 16 non-structural proteins in the SARS-CoV-2 ~30 000-bp genome,[9] the gene looked to most is the S gene responsible for the spike protein. The spike protein is a 1273 amino acid long (YP_009724390.1)(NC_045512) surface protein that is the viral component accountable for interacting with the human angiotensin-converting enzyme 2 (ACE2) (UNIPROT ID Q9BYF1).[7,12-14] ACE2, genetically encoded on the human X chromosome (ENSG00000130234), is a component of the renin-angiotensin hormone system in humans and is ultimately a vasodilator.[15,16] This interaction between SARS-CoV-2 spike protein and human ACE2 via the receptor-binding domain (RBD) allows SARS-CoV-2 to enter cells and infect the human host.[12] Mutations in the spike protein can alter binding efficiency and viral fitness.[10] Indeed, some nucleotide mutations in the SARS-CoV-2 S gene change pathogenicity,[12] affect viral fitness,[10,17] reduce virulence,[1,4] and have become commonplace in tracking the spread of SARS-CoV-2.[17] These S gene and spike protein mutations can increase transmission of the virus between hosts through anatomical localization to the upper respiratory tract.[10] Therefore, to understand the SARS-CoV-2 pathogenicity, it is important to characterize the virus mutations to study viral pathogenesis and vaccine development. In this study, we report analysis of a 969-bp SARS-CoV-2 S gene from 2 patients from Hawai‘i to understand the changes in the spike protein, a target for vaccines.

## Methods

### Patient Samples and Viral RNA Extraction

The 2 patients (patient identification [PID] 00498 and PID 00708) analyzed in this report were part of the University of Hawai‘i at Mānoa Institutional Review Board (IRB)-approved H051 study (IRB# 2020-00367). Patient PID 00498 and patient PID 00708 are both males, 1 identifies as white, and the other identifies as Japanese, Okinawan, and Filipino; their mean age is 29.5 years. These patients were previously identified as having SARS-CoV-2, and oropharyngeal swab (OS - PID 00498) and nasal swab (NS - PID 00708) were collected in August 2020, 3 days after first polymerase chain reaction (PCR) positive diagnosis. Samples were stored at -80°C. Neither of the patients had traveled outside of Honolulu in the week before their first PCR positive SARS-CoV-2 diagnosis, however, both identified potential sources of exposure in Honolulu.

Swabs stored in viral transport media (VTM) at -80°C were thawed in the biosafety cabinet at the John A. Burns School of Medicine high containment laboratory as part of the University of Hawai‘i at Mānoa Institutional Biosafety Committee (IBC)-approved study (IBC#20-04-830-05). VTM was centrifuged to separate the supernatant from debris, aliquoted, and 140 µL of the VTM was used for viral RNA purification using the QIAamp® Viral RNA Mini Kit (Cat# 52906) following the manufacturer›s instructions. The samples were eluted in 30 µL of the elution buffer.

### Reverse Transcriptase Polymerase Chain Reaction and Sequencing

As per the manufacturer's instructions, purified viral RNA was transcribed into cDNA using the Takara RNA LA PCR Kit (Cat #RR012A) with random 9 mers and an extension time of 90 minutes. Primer sets were designed based on published sequences and were procured from Integrated DNA Technologies (Coralville, IA). A 1127-bp segment of the S gene was amplified using the Takara RNA LA PCR Kit (Cat #RR012A) and primers CF and CR (Figure 1).[18] PCR was conducted according to the manufacturer's instructions and cycled on the Applied Biosystems GeneAmp® PCR System 9600. PCR products were then electrophoresed on 1.5% agarose 1x TBE gels at 50V, and the amplicons of interest were purified using the Qiagen QIAquick Gel Extraction Kit (Cat# 28704).

Sanger sequencing was conducted on the amplicons using 4 primers (CF, CR,[18] CR2, and CR3) at the Advanced Studies in Genomics, Proteomics, and Bioinformatics (ASGPB) core facility at the University of Hawai‘i at Mānoa (Figure 1). The resulting sequences were input into and verified using both MEGAX[19,20] and SnapGene software (Insightful Science, www.snapgene.com) and aligned using Multiple Sequence Comparison by Log-Expectation (MUSCLE) program[21] to define the contiguous sequence. The resulting 969-bp consensus sequences were uploaded to the National Center for Biotechnology Information (NCBI) database. The S gene 969-bp region encompasses nucleotides 23 042 to 24 010 and corresponds to amino acids 494 to 816, which involves the 3' and C-terminal of the RBD that ends at nucleotide 23 185 and amino acid 541.[7]

### Single Nucleotide Polymorphism (SNP) Analysis

Sixty-eight coronavirus strains representing alpha and beta lineages were selected from the NCBI database representing 25 distinct geographical locations spanning the pandemic duration and at least 1 SARS-CoV-2 strain per month from December 2019 to September 2020. Of these 68 coronavirus strains, 55 were SARS-CoV-2 strains. All SARS-CoV-2 sequences, including previously published Hawai‘i sequences, were first aligned, and redundant sequences were removed from further analysis.

Coronavirus sequences were aligned with the 969-bp S gene region with SnapGene using MUSCLE, and the corresponding region was used for future analysis.[21] The non-SARS-CoV-2 strains were removed if the 969-bp S gene of SARS-CoV-2 sequence did not align with the S gene of the non-SARS-CoV-2 strains. Based on the alignment, SNPs were identified and annotated into SnapGene to analyze the amino acid substitutions.

Upon finding the P681H mutation among the 2 Hawai'i strains in this study, the Global Initiative of Sharing All Influenza Data (GISAID) database[22,23] was used to filter worldwide SARS-CoV-2 sequences by the P681H mutation to create a ratio of sequences containing the P681H mutation to all sequences reported in the GISAID database for a given month. Inclusion criteria were for sequences providing a full month, day, and year. The D614G mutation underwent assessment in the same manner for comparison. All prevalence data converted into ratio underwent a logarithmic transformation. Pearson's correlation tests between P681H frequency versus month, D614G frequency versus month, and P681H frequency versus D614G frequency were conducted and verified using GraphPad Prism version 9.0.0 for Mac (GraphPad Software, San Diego, California USA, www.graphpad.com), JASP version 0.14,[24] and RStudio version 1.3.1093 (R version 4.0.3).[25]

### Phylogenetic Tree

After the SNP analysis, incomplete sequences were removed before the construction of the phylogenetic tree. The phylogenetic tree was constructed using MEGAX.[19] The alignment was first done using the program MUSCLE.[21] The phylogenetic tree was then generated with Maximum Likelihood parameters with 1,000 bootstraps in MEGAX[19,20] using the University of Hawai'i MANA High Performance Computing Cluster. The output tree from MEGAX was rooted using FigTree version 1.4.4 based on alpha coronavirus human 299E (KF514433).[26]

## Results

### Gene Amplification and Sequence Analysis

SARS-CoV-2 genomic sequences were detected by reverse transcriptase-polymerase chain reaction (RT-PCR) in both the patients, PID 00498 and PID 00708, using various primers spanning the S gene (Figure 1). A 1127-bp segment was amplified and sequenced, and the entire sequence of the amplicon was aligned with at least 1 forward and 1 reverse sequence (translated into reverse-complement) to span the whole 1127-bp region. For final sequence analysis, a 969-bp sequence verified by sequencing the 5' and 3' ends was used. The 2 Hawai'i sequences were deposited in the GenBank, accession numbers MW237663 for PID 00498 and MW237664 for PID 00708.

### SNP Analysis

Of the 55 original non-Hawai'i SARS-CoV-2 strains, 47 were redundant in the 969-bp segment of the S gene. Of the 12 Hawai'i strains deposited in the GenBank, 9 were redundant in the 969-bp sequence region. Thus, we analyzed 8 non-Hawai'i SARS-CoV-2 strains and 3 SARS-CoV-2 strains from Hawai'i. With the addition of the 2 SARS-CoV-2 strain sequences from this study, a total of 13 SARS-CoV-2 sequences were compared, and SNPs encompassing the 969-bp region of the S gene were analyzed (Table 1). The alignment containing the 13 sequences revealed 13 SNPs (Table 1) (Figure 1). Eleven of the 13 mutations resulted in non-synonymous mutations (A522S, F543L, R577C, I584V, D614G, S680C, P681H, I726F, A771S, E780Q, and F797C) (Table 1 and Figure 1). Two of the 13 mutations resulted in a synonymous mutation (amino acid 541 and 790) (Table 1 and Figure 1). The P681H mutation is unique to the Hawai'i strains from this study (MW237663 and MW237664).

GISAID reported the first P681H mutation on March 12, 2020 (EPI_ISL_430887).[27] Further, from March 01, 2020, through January 31, 2021, GISAID reports a total of 65 959 strains that have the P681H mutation. During that same time, GISAID has reported approximately 480 822 SARS-CoV-2 strains (Table 2). Pearson's correlation between time in months versus prevalence of P681H (Figure 2A) and D614G (Figure 2B) of logarithmically transformed data indicates an increase in the number of strains having the P681H mutation ($r$=0.97, $P$ <.0001) (Figure 2A) and plateauing of the D614G mutation ($r$=0.77, $P$=.005) (Figure 2B). P681H mutations were not reported in May 2020. Further, Pearson's correlation indicates a positive correlation ($r$=0.69, $P$=.03) between the worldwide prevalence of P681H and D614G (Figure 2C).

### Phylogenetic Tree

Of the 13 SARS-CoV-2 sequences used for SNP identification, 2 were incomplete due to unidentified nucleotides and were removed from the phylogenetic analysis. Similarly, of the 13 non-SARS-CoV-2 sequences, 4 did not align to the 969-bp S gene due to large insertions or deletions and were removed from further analysis. Therefore, the final phylogenetic tree was constructed using 20 coronavirus sequences, 11 SARS-CoV-2, and 9 non-SARS-CoV-2 sequences (Figure 3). Based on the phylogenetic tree constructed using the Maximum Likelihood method, the alpha and beta coronaviruses segregated as expected. Further, the beta coronaviruses lineages A, B, C, and D segregated with a bootstrap value of >70. Within the beta coronavirus lineage B, the SARS-CoV-1 and the bat coronaviruses were distinctly segregated from the SARS-CoV-2 with a bootstrap value of 92.

Within the SARS-CoV-2 branch of beta coronavirus lineage B, the D614G mutation was the defining node for branch separation. The 3 sequences lacking the D614G mutation (NC_045512, MT344949, and MT093571) are separated from sequences with the D614G mutation with a bootstrap value of 100, except for the MW066483 Hawai'i sequence, which also does not have the D614G mutation. Wuhan (NC_045512)

and Hawai‘i (MT344949) strains are identical and contain no mutations, as NC_045512 is the reference genome for SARS-CoV-2. The Sweden strain (MT093571) has a F797C mutation. The Hawai‘i strain MW064483 is the next closest cluster to the D614G defining node and additionally contains the synonymous tyrosine mutation at amino acid 790. All the remaining sequences have the D614G mutation. Clustering near the Hawai‘i strain MW066483 are 2 strains from the state of New York (MW035565 and MW035511), both containing the E780Q mutation and MW035565 also containing the A522S mutation and a synonymous phenylalanine mutation at amino acid 541. Branching from the New York strains cluster is a strain from the state of Washington (MT994395), exclusively having the I584V mutation. The 2 Hawai‘i strains from this study (MW237663 and MW237664) have the emerging P681H mutation and cluster closely with previously published SARS-CoV-2 sequences from Hawai‘i (MT627421) and China (MT407659). MT627421 strain from Hawai‘i and MT407659 strain from China are identical and are the only sequences to contain the D614G mutation exclusively.

In summary, SARS-CoV-2 strains from Hawai‘i deposited in the GenBank in March 2020 clustered with sequences from Wuhan, Sweden, China, and the state of New York. The SARS-CoV-2 strains in this study cluster from the state of Washington and with sequences from China and Hawai‘i. Five of the 13 SARS-CoV-2 sequences used in the phylogenetic tree are sequences from Hawai‘i, marked with an asterisk. Coronavirus lineage determinations are based on phylogenetic trees constructed by Chan and colleagues[28] and Su and colleagues.[29]

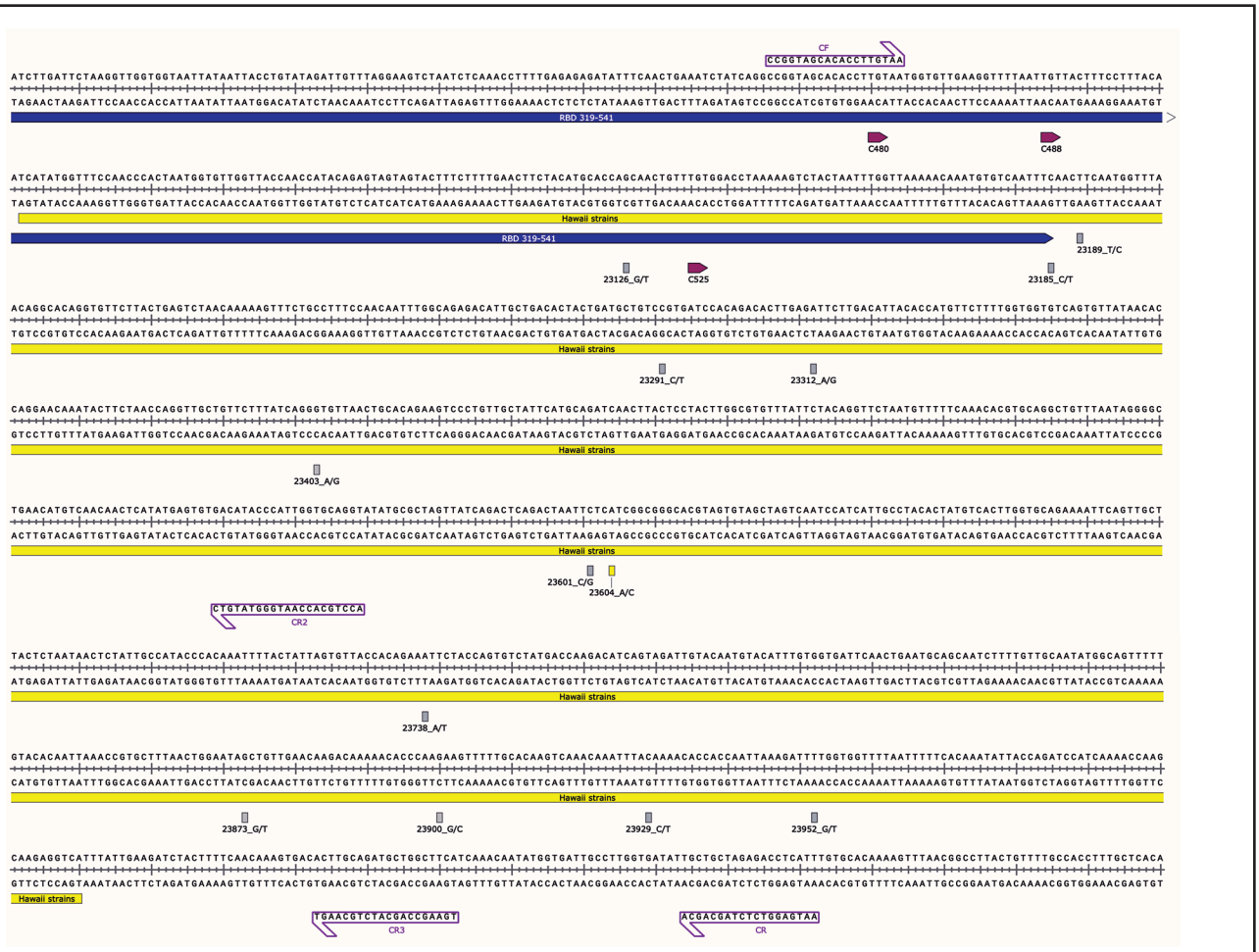


Figure 1. SARS-CoV-2 S Gene Region used in this Study Along with Annotated Primers, Mutations, and Cysteine Residues of the Receptor Binding Domain

This figure represents the Hawai‘i strain MW237663 and MW237664 sequences. The primer pair, CF/CR, was used to amplify the 1127-bp S gene fragment, and primers CF, CR, CR2, and CR3 depicted with purple boxes were used for Sanger sequencing. The yellow box indicates the start and end of the 969-bp sequence. The blue line indicates the 3’ end of the S gene receptor-binding domain (RBD). RBD cysteine residues are shown in depicted boxes. All mutations found in this study are in their respective loci with nucleotide numbers, and rectangular boxes correlating to the sense strand as indicated after the nucleotide number and underscore in the figure (nucleotide/protein mutations: G23126T/A522S, C23185T/F541F, T23189C/F543L, C23291T/R577C, A23312G/I584V, A23403G/D614G, C23601G/S680C, C23604A/P681H, A23738T/I726F, G23873T/A771S, G23900C/E780Q, C23929T/Y790Y, and T23952G/F797C). All boxes are grey except for the P681H mutation seen in the Hawai‘i strains from this study, shown with a yellow rectangle. Image was generated with the SnapGene software (from Insightful Science; available at www.snapgene.com) and was created with BioRender.com.

Table 1. Comparison of Single Nucleotide Polymorphisms and Resultant Amino Acid Substitutions in a 969-bp S gene of SARS-CoV-2 Strains from Hawai'i

| ACCESSION AND IDENTIFIER | SNP | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 23126 NT | 522 AA | 23185 NT | 541 AA | 23189 NT | 543 AA | 23291 NT | 577 AA | 23312 NT | 584 AA | 23403 NT | 614 AA | 23601 NT | 680 AA | 23604 NT | 681 AA | 23738 NT | 726 AA | 23873 NT | 771 AA | 23900 NT | 780 AA | 23929 NT | 790 AA | 23952 NT | 797 AA |
| MW237663_HI | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | **A** | **His** | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| MW237664_HI | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | **A** | **His** | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| MW064483.1_HI | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | A | Asp | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | **T** | **Tyr** | T | Phe |
| MT627421_HI | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| MT344949_HI | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | A | Asp | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| NC_045512.2_CHN | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | A | Asp | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| MT407659.1_CHN | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| MW035565_NY | **T** | **Ser** | **T** | **Phe** | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | C | Pro | A | Ile | G | Ala | **C** | **Gln** | C | Tyr | T | Phe |
| MW035511_NY | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | C | Pro | A | Ile | G | Ala | **C** | **Gln** | C | Tyr | T | Phe |
| MT994395_WA | G | Ala | C | Phe | T | Phe | C | Arg | **G** | **Val** | **G** | **Gly** | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |
| MT093571.1_SWE | G | Ala | C | Phe | T | Phe | C | Arg | A | Ile | A | Asp | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | **G** | **Cys** |
| MT451798.1_AUS | N | - | C | Phe | **Y** | **Leu/ Phe** | **Y** | **Arg/ Cys** | A | Ile | A | Asp | **S** | **Ser/ Cys** | C | Pro | **W** | **Ile/ Phe** | **K** | **Ala/ Ser** | G | Glu | C | Tyr | T | Phe |
| MT394864.1_DEU | N | - | C | Phe | T | Phe | C | Arg | A | Ile | **G** | **Gly** | C | Ser | C | Pro | A | Ile | G | Ala | G | Glu | C | Tyr | T | Phe |

Abbreviations: HI, Hawai'i; CHN, China; NY, New York; WA, Washington; SWE, Sweden; AUS, Australia; DEU, Germany;
SNP, Single Nucleotide Polymorphism; NT, nucleotide; A, Adenine; C, Cytosine; G, Guanine; T, Thymine; K, Guanine or Thymine; S, Guanine or Cytosine; W, Adenine or Thymine; Y, Cytosine or Thymine;
AA, Amino Acid; Ala, Alanine; Arg, Arginine; Asp, Aspartic Acid; Cys, Cysteine; Gln, Glutamine; Glu, Glutamic Acid; Gly, Glycine; His, Histidine; Ile, Isoleucine; Leu, Leucine; Phe, Phenylalanine; Pro, Proline; Ser, Serine; Tyr, Tyrosine; Val, Valine

Table 2. The Distribution and Frequency of P681H and D614G Mutations Among All SARS-CoV-2 Sequences by Month Reported in the GISAID Database in Year 2020 and 2021

| Month and Year | n | P681H n (%) | D614G n (%) |
|---|---|---|---|
| March 2020 | 47 120 | 9 (0.02%) | 34 375 (73.0%) |
| April 2020 | 44 386 | 8 (0.02%) | 37 782 (85.1%) |
| May 2020 | 22 230 | 0 (0%) | 20 412 (91.8%) |
| June 2020 | 23 975 | 14 (0.06%) | 23 126 (96.5%) |
| July 2020 | 22 917 | 53 (0.2%) | 22 285 (97.2%) |
| August 2020 | 25 439 | 229 (0.9%) | 25 094 (98.6%) |
| September 2020 | 29 831 | 223 (0.8%) | 29,674 (99.5%) |
| October 2020 | 50 910 | 407 (0.8%) | 50 672 (99.5%) |
| November 2020 | 59 650 | 2701 (4.5%) | 59 495 (99.7%) |
| December 2020 | 73 405 | 18 347 (25.0%) | 72 868 (99.3%) |
| January 2021 | 80 959 | 43 968 (54.3%) | 80 516 (99.4%) |

Abbreviations: GISAID, Global Initiative of Sharing All Influenza Data

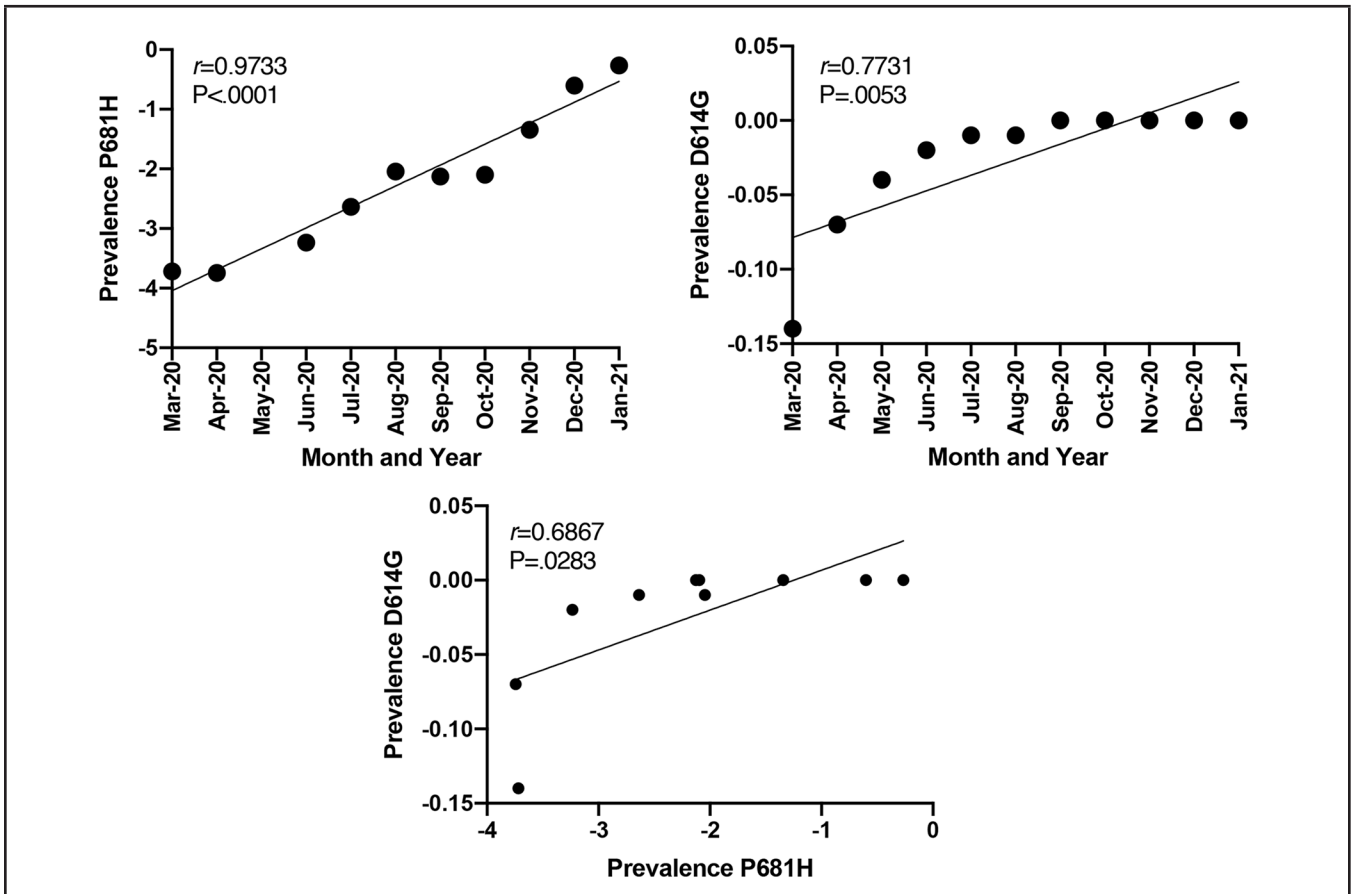


Figure 2. Pearson's Correlation of Logarithmically Transformed Data Showing Positive Correlation for Time in Months Versus Both P681H and D614G Mutations

(A) Graphical representation of the logarithmic transformed ratio of P681H mutation among all reported Global Initiative of Sharing All Influenza Data (GISAID) strains on the y-axis and month on the x-axis. Linear regression line shown along with Pearson's correlation, r=0.97, P=2.157e-06. (B) Graphical representation of the logarithmic transformed ratio of D614G mutation among all reported GISAID strains on the y-axis and month on the x-axis. Linear regression line shown along with Pearson's correlation, r=0.77, P=.005. (C) Graphical representation of the logarithmic transformed ratio of D614G mutation among all reported GISAID strains on the y-axis and the logarithmic transformed ratio of P681H mutations among all reported GISAID strains on the x-axis. Linear regression line shown along with Pearson's correlation, r=0.69, P=.03. Graphs were created with GraphPad Prism version 9.0.0 for Mac (GraphPad Software, San Diego, CA; www.graphpad.com).

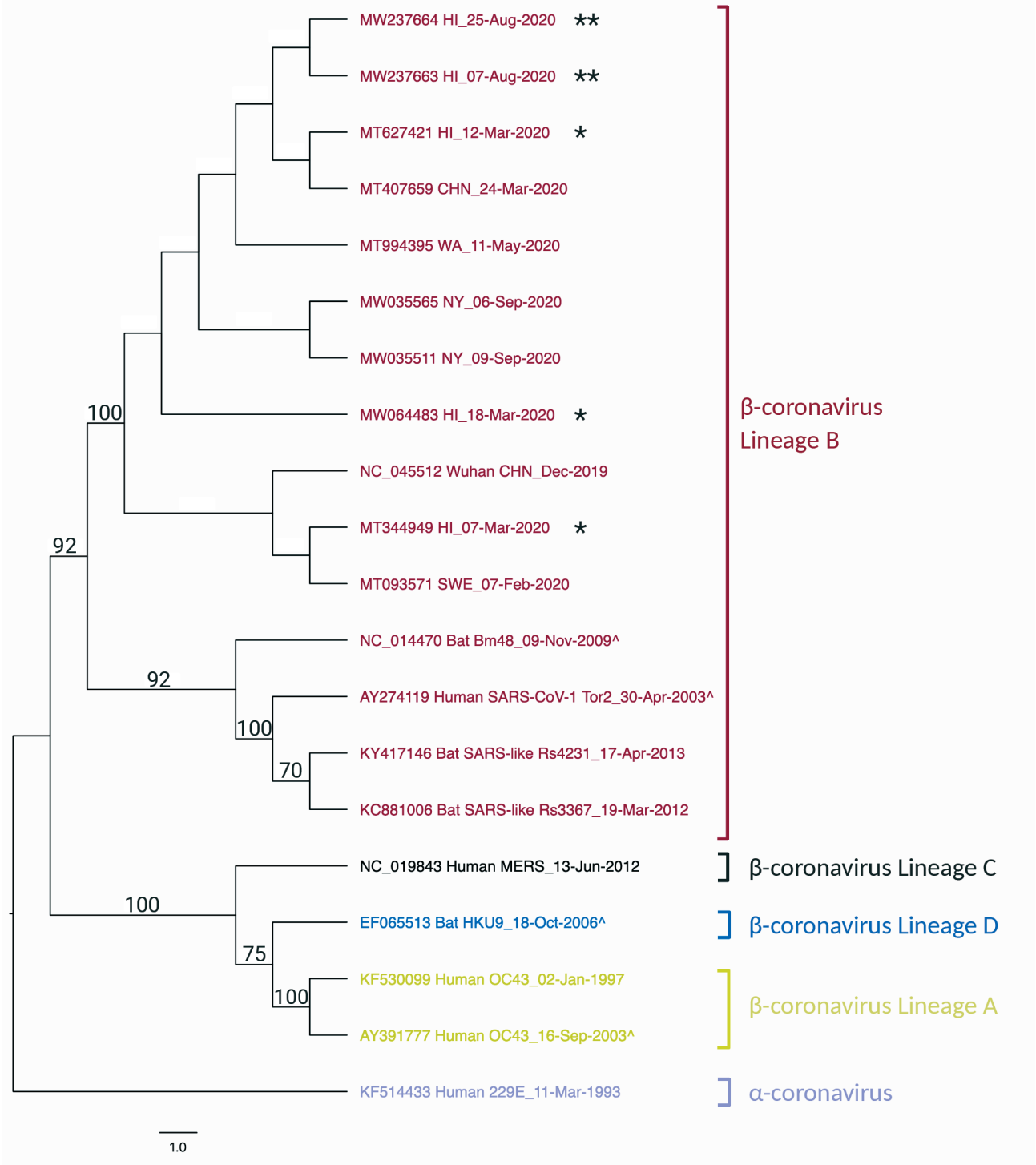


Figure 3. Maximum Likelihood Phylogenetic Tree Constructed Using a 969-bp S gene Region of SARS-CoV-2

The Tamura-Nei model and the Maximum Likelihood method were used to infer evolutionary history using 1000 bootstraps. The tree with the highest log-likelihood is shown in the figure. Next to the branches is shown the percentage of trees in which the associated taxa clustered together; only values greater than 70 are displayed. Neighbor-Join and BioNJ algorithms were applied to a matrix of pairwise distances estimated using the Tamura-Nei model to automatically obtain the initial tree for the heuristic search and then selecting the topology with superior log likelihood value. This analysis involves nucleotide sequences from 20 taxa. There were a total of 1366 final dataset positions. Evolutionary analyses were conducted in MEGAX19,20 using the University of Hawai'i MANA High-Performance Computing Cluster. The tree was rooted using the alphacoronavirus human 229E (KF514433) taxa in FigTree version 1.4.4. Yellow text is used for betacoronavirus lineage A, red text denotes betacoronavirus lineage B, black text denotes betacoronavirus lineage C, blue text shows betacoronavirus lineage D, and purple text is for alphacoronavirus.

* represents strains from Hawai'i. ** represents strains from this study. ^ indicates sequence submission date rather than collection date. Created with BioRender.com.

## Discussion

This report focuses on SARS-CoV-2 strains from 2 patients in Hawai‘i based on a 969-bp S gene. The sequence and phylogenetic analysis indicate and support that the S gene is continuously mutating as previously reported,[30] and Hawai‘i may be harboring a unique strain with an emerging mutation in an altered spike protein. Analysis of the SNPs found in the 969-bp S gene region indicates the loss of a proline residue and the gain of cysteine residues. These mutations potentially alter the spike protein monomeric and trimeric structures.

The P681H represents the loss of a proline residue and the gain instead of an imidazole-containing histidine residue. According to the GISAID database, the P681H mutation is found worldwide in 65 959 strains reported as of January 31, 2021. The Pearson's correlation test of the logarithmic transformed P681H prevalence of the mutation versus time indicates that the P681H mutation is exponentially increasing worldwide, and the sequences encompassing the P681H mutation are dominating significantly when compared to other SARS-CoV-2 strains. This significant finding suggests that there is a selective pressure in favor of this mutation.

A study looking at the effect of the loss of a proline residue in the spike protein of the mouse hepatitis virus, a coronavirus, observed altered pathology, fusion kinetics, and enhanced infectivity.[31] The same study also suggests that prolines in regions adjacent to RBDs may not be essential for fusion but may significantly change structure and function of the spike protein.[31] Recent SARS-CoV-2 studies indicate that the P681H mutation is immediately juxtaposed to the amino acid 682–685, furin cleavage site, identified at the S1/S2 linkage site, which predicted enhance systemic infection,[12,32] and increased membrane fusion.[11] Additionally, the proline in the P681H mutation is within the epitope found to be the highest-ranking B and T cell epitope based on the in silico long-term population-scale epitope prediction for vaccine development study.[11] Therefore, the sequence surrounding this P681H mutation is predictably the loci where the immune response is targeted, meaning this mutation could be the first identified SARS-CoV-2 mutation of antigenic evolution.[1] Further studies are warranted to analyze the pathogenicity and virulence of the newly identified P681H mutation seen in the Hawai‘i strains and whether this is a viral evasion mechanism to deter antibody recognition or another increase in fitness. Now that SARS-CoV-2 vaccines are available in the United States under the Food and Drug Administration-Emergency Use Authorization (FDA-EUA), it is critical to evaluate the epitope-altering mutations. These mutations could change the effectiveness of FDA-EUA SARS-CoV-2 vaccines that rely on the structure of the spike protein.[33,34]

Twelve full length sequences have been published from Hawai‘i (MT627420.1, MT627421.1, MW064481.1, MW064482.1, MW064483.1, MW064596.1, MW064825.1, MW064826.1, MW065225.1, MW190887.1, MT344948.1, MT344949.1). All of these original strains introduced to Hawai‘i were collected in March 2020, and 66.6% (8 of 12) have the D614G mutation. The D614G mutation has become universal throughout the SARS-CoV-2 strains.[10] The D614G mutation is known to enhance infectivity and replication and localize the virus to the upper respiratory tract to increase transmission.[10,17] Interestingly, several mutations (nucleotide position 241 C→T, position 3037 C→T, and position 14 408 C→T, etc) exist alongside the D614G mutation[10,17] Similarly, in both Hawai‘i SARS-CoV-2 strains, the P681H mutation is also present alongside D614G.[10,13,17] This observation indicates that similar to the D614G mutation, the P681H mutation is becoming globally prevalent among SARS-CoV-2 sequences.

The R577C, S680C, and F797C mutations depicted in Table 1 are also very prominent mutations in that they present possible new disulfide bridges forming within and around the RBD. The RBD possesses 8 cysteine residues, with disulfide bridges formed between amino acids 336:361, 379:432, 480:488, and 391:525.[7,14] The aforementioned cysteine mutations may interact with these known bridges or create new bridges. The F797C mutation is seen alone in the Sweden strain (MT093571.1). The R577C and S680C mutations are present together in the strain from Australia (MT451798.1). Similar to the P681H, the S680C mutation is also within the epitope region of the B and T cell epitope in silico prediction model for vaccine development.[11] Further studies are warranted to evaluate the disulfide bridge configurations and whether an odd number of cysteines in this region can result in a dynamic bridge or the addition of several cysteines can alter the spike protein structure. Such studies would help to understand if these mutations are evolutionary mechanisms that alter virulence, or perhaps influence fusion kinetics. The other non-synonymous SNPs found in this study (A522S, F543L, I584V, I726F, A771S, E780Q) are not as apparent in presenting drastic evolutionary change, but they too deserve further analysis.

Recently, the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) group based out of London, England, has reported on a new SARS-CoV-2 variant (variant of concern [VOC] 202012/01).[35,36] NERVTAG reports that the variant has increased transmissibility, and further studies are underway to confirm their report.[37] This variant includes amino acid mutations in ORF1ab, spike, Orf8, and N.[35,37,38] The 6 ORF1ab mutations are T1001I, A1708D, I2230T, and ΔS3675, ΔG2676, and ΔF3677.[35,37,38] The 10 spike mutations are ΔH69, ΔV70, ΔY145, N501Y, A570D, D614G, P681H, T716I, S982A, and D1118.[35,37,38] The Orf8 mutations are Q27stop, R52I, and Y73C.[37,38] The N protein mutations are D3L and S235F.[37,38] When comparing the SNPs encompassing the 969-bp of 2 strains from this study to the reference genome for VOC202012/01, EPI_ISL_601443,[39] we found 2 similar mutations, D614G and P681H.[37] Further, EPI_ISL_601443 shows the N501Y, A570D, D614G, P681H, and T716 mutations in the 969-bp region, while

the 2 Hawai‘i strains, MW237663 and MW237664, display the D614G and P681H mutations. Additionally, a new variant in Nigeria (B.1.1.207)(EPI_ISL_729975)[40] has been defined by the P681H mutation found in the 2 Hawai‘i strains.

The 2 Hawai‘i strains analyzed in this study cluster together predictably due to the emerging P681H mutation. These 2 strains also cluster closely with a strain from China and a previously published Hawai‘i strain. Other previously published Hawai‘i strains cluster with SARS-CoV-2 strains from New York, Wuhan, Sweden, and China. These analyses and resultant phylogenetic tree indicate that the virus has likely been introduced to Hawai‘i through several sources.

Over the past year, SARS-CoV-2 worldwide has evolved and will continue to do so. As of this report's publication, 6 new SARS-CoV-2 variants have been reported from the United Kingdom (B.1.1.7/VOC 202012/01),[41] South Africa (B.1.351/501Y.V2),[41] Denmark (B.1.1.298/Mink Cluster V),[42,43] Nigeria (B.1.1.207),[41] Brazil (B.1.1.248/P.1),[44] and California (B.1.429/L452R).[45] This fast pace of evolutionary changes will affect pathogenicity of SARS-CoV-2[12,46] and warrants further in silico, in vitro, and in vivo studies.

In summary, COVID-19 in Hawai‘i and the pandemic originating in Wuhan in the 2019–2020 winter is still ongoing. The virus continues to mutate, and the effects and outcomes of several of these mutations have yet to be elucidated. This study demonstrates a partial sequence from the first SARS-CoV-2 strain possessing the P681H non-synonymous mutation. In Hawai‘i, Native Hawaiians and Pacific Islanders have a significantly high prevalence of SARS-CoV-2 compared to other ethnic minorities and whites.[47] Therefore, characterizing viral sequences from these minority groups is important to understand virus transmission and pathogenicity better.

## Conflicts of Interest

None of the authors identify a conflict of interest.

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# The Role of a 6-Month Primary Care Mentorship Program on Medical Student Residency Specialty

Nash A.K. Witten MD and Gregory G. Maskarinec PhD

## Abstract

*Primary care is the greatest physician specialty shortage area nationally and in the State of Hawai'i, and the shortage is expected to worsen in the coming years. During the 2015–2016 academic year, a 6-month Primary Care Mentorship Program (PCMP) for first-year medical students was launched at the John A. Burns School of Medicine (JABSOM). This study sought to determine (1) whether participation in a PCMP as a first-year medical student correlates with an increased likelihood of matching into a primary care graduate medical education (GME) residency specialty, (2) whether the PCMP medical student participants developed lasting mentorship relationships with their assigned mentor, and (3) whether a PCMP is a worthwhile endeavor for medical schools to incorporate into their structured undergraduate medical education curriculum. Mentees were surveyed before and after the PCMP and after the residency Match. Overall, 105 (36%) of the 288 students in the JABSOM classes of 2019–2022 have applied to participate in the PCMP. Seventeen (85%) of the 20 JABSOM class of 2019 PCMP mentees completed the post-Match reflection survey. The study found as follows: (1) participation in a 6-month PCMP as a first-year medical student does not correlate with an increased likelihood of matching into a primary care GME residency specialty, (2) 7 (41%) participants did continue their mentorship relationship following completion of the PCMP, and (3) overwhelmingly positive qualitative feedback from mentees and the number of mentees who did establish lasting mentorship relationships suggest a PCMP is a worthwhile endeavor for medical schools to implement.*

## Keywords

*primary care issues, mentoring, undergraduate medical education*

## Abbreviations

*GME = graduate medical education*
*JABSOM = University of Hawai'i John A. Burns School of Medicine*
*PCMP = Primary Care Mentorship Program*
*PCP = Primary Care Progress*

## Introduction

Primary care is the greatest physician specialty shortage area nationally and in the State of Hawai'i. As of 2018, Hawai'i had a shortage of 263 full-time equivalent primary care physicians spread across every island and in both urban and rural communities. The demand for additional primary care providers is expected to worsen in coming years.[1] The University of Hawai'i John A. Burns School of Medicine (JABSOM), through its undergraduate and graduate medical education programs, has produced about half of all physicians practicing in Hawai'i today.[2] Researchers have attempted to better understand the factors that influence medical student specialty choice to inform medical schools to meet the primary care physician shortage.[3,4] Numerous factors play a role in medical student specialty choice: (1) social compassion, attitudes, and values; (2) financial considerations; (3) family and personal concerns; (4) subjective and reinforcing influences; and (5) medical training experiences.[5] An important factor in multiple studies is the role of faculty mentorship in medical student specialty choice.[4–8] The Office of Student Affairs at JABSOM has had some form of formal mentorship program for medical students since 2009. During the 2015–2016 academic year, the mentorship program was called "Pod-vising" and consisted of medical students from all 4 medical school classes and faculty advisors. Each "Pod" group met once a quarter for 1 hour to provide peer and faculty group mentorship.[9]

During the 2014–2015 academic year, a Primary Care Progress (PCP) chapter was founded at JABSOM. PCP, a non-profit company based out of Boston, Massachusetts, has a mission to promote "leadership development and community building," and as part of that mission, the new JABSOM PCP chapter held a town hall meeting to assess what was keeping medical students from entering a career in primary care.[10] The overwhelming theme from the town hall meeting was a lack of actively working, engaged, and enthusiastic primary care physician mentors for medical students. To assist JABSOM in producing more students entering primary care specialties, the JABSOM PCP chapter created a Primary Care Mentorship Program (PCMP) during the 2015–2016 academic year. The 6-month program paired first-year medical students with community primary care physicians in the specialties of Family Medicine, Internal Medicine, and Pediatrics. The PCMP encouraged 6 half-day clinical shadowing experiences, 6 telephone or email communications, and attendance at JABSOM PCP events. Upon completing the 6-month PCMP, each participant received a certificate of completion. Due to the success of the initial 6-month program, it has been continued since the inaugural cohort in Fall 2015.

The goals of this study were to determine

(1) whether participation in a PCMP as a first-year medical student correlates with an increased likelihood of matching into a primary care graduate medicine education (GME) residency specialty;

(2) whether the PCMP medical student participants developed lasting mentorship relationships with their assigned mentor; and

(3) whether a PCMP is a worthwhile endeavor for medical schools to incorporate into their structured undergraduate medical education curriculum.

## Methods

The JABSOM classes of 2019–2022 were emailed an application to participate in the program in the fall and spring of their first year of medical school. Community primary care physicians were also emailed an application to participate in the program before each 6-month PCMP cohort (Appendix 1). First-year medical students were then paired by the PCP PCMP leadership team based on medical student primary care specialty of interest, as feasible. Upon completing each 6-month PCMP, each medical student and community primary care physician was emailed a post-participation survey containing quantitative and qualitative questions (Appendix 2 and 3). In Spring 2019, the first 2 PCMP cohorts successfully matched into GME residency specialties. The National Resident Matching Program is a private, non-profit organization that provides a fair mechanism for United States fourth-year medical students to pair with a graduate medical specialty and releases the pairing result, called "The Match," in the spring of each academic year.[11] After "The Match," a reflection survey containing both qualitative and quantitative questions was emailed to JABSOM class of 2019 PCMP cohort participants regarding their experience in the PCMP and the remainder of training in medical school (Appendix 4). Quantitative data were analyzed to address goal (1) of the study using Microsoft Excel version 16.16.6 (Microsoft; Redmond, Washington), including mean with standard deviation [SD], median, and mode; and two-sample t-test assuming equal variances. Qualitative analysis was conducted on the data to determine goals (2) and (3) of the study. The study was submitted and approved by the University of Hawai'i Institutional Review Board for Human Research (IRB 2018-00742).

## Results

Overall, 105 (36%) of the total 288 students in the JABSOM classes of 2019–2022 have applied to participate in the program as first-year medical students, assuming 72 JABSOM students per class, as seen in Table 1.[12] Forty-three medical student applicants were interested in finding a primary care Internal Medicine mentor, while 32 indicated an interest in Family Medicine and 21 indicated an interest in Pediatrics. Of the 105 medical student applicants, 13 were unable to be paired with a mentor due to a lack of mentor availability, as seen in Table 2. Ninety-two first-year medical student participants were successfully paired with community physician mentors: 47 with Internal Medicine, 30 with Family Medicine, and 15 with Pediatric community physicians.

Upon completing the 6-month PCMP, 32 (30%) of first-year medical student participants completed the feedback survey. The mean number of shadowing experiences medical students had during the program was 2, with a mode of 1. The most common issue expressed by medical students concerning shadowing was difficulty scheduling, primarily due to the lack of available time during the week. Twenty-nine (91%) of the 32 medical students communicated with their mentors outside of clinic shadowing via email, while 17 (53%) had face-to-face meetings, and 8 (25%) had phone calls. Medical students also gained a better understanding of the reality of being a primary care physician, with one mentee stating, "[My mentor] taught me that the best doctors are ones that take the time to really connect with patients and provide them with the education and information to allow them to make their own informed decisions regarding their health care." Other feedback regarding insight into primary care provided by the PCMP include "You don't ONLY see 'coughs and colds,'" "I aspire to become a caring physician who gains her patients' trust, just like how my mentor had done," and "I believe that it is one of the most important fields in medicine." Other positive themes expressed included the benefit of flexibility in clinic scheduling, the number of career options, the complexity of chronic disease management, and the breadth of knowledge needed. Negative themes included the frustrating and complicated coordination of patient care, the number of patients needed to be seen per day, the high overhead cost of private practice, patient non-compliance, the volume of paperwork, and complex reimbursements from insurance companies' services.

Table 1. JABSOM PCP PCMP Mentee Applications, JABSOM Classes of 2019–2022.

| JABSOM Class | No Preference n (%) | Mentor Specialty | | | Total n (%) |
|---|---|---|---|---|---|
| | | Family Medicine n (%) | Internal Medicine n (%) | Pediatrics n (%) | |
| 2019 | 4 | 5 | 10 | 3 | 22 |
| 2020 | 2 | 12 | 10 | 6 | 30 |
| 2021 | 3 | 7 | 9 | 8 | 27 |
| 2022 | 0 | 8 | 14 | 4 | 26 |
| Total | 9 (9%)[a] | 32 (30%)[a] | 43 (41%)[a] | 21 (20%)[a] | 105 (36%)[b] |

Abbreviations: JABSOM. University of Hawai'i John A. Burns School of Medicine; PCMP, Primary Care Mentorship Program; PCP, Primary Care Progress.

[a] Total number of JABSOM students who selected a mentor in a particular primary care specialty versus no preference in mentor primary care specialty divided by the total number of JABSOM students who participated in the PCMP (105).

[b] Total number of JABSOM students who selected a mentor in a particular primary care specialty versus no preference in mentor primary care specialty (105) divided by the total number of JABSOM students per class between 2019–2022 (288), assuming 72 students per year, the average class size increased during the study period (University of Hawai'i John A. Burns School of Medicine. Admitted Class Profile. https://admissions.jabsom.hawaii.edu/prospective-students/admitted-class-profile/)

The mode rating for mentee experience in the PCMP was 4 out of 5, with 5 being a life-altering experience. Additional qualitative feedback from mentees regarding their experience overall was positive, with numerous mentees expressing that the PCMP was a "valuable experience," "great program," and that they would "love to participate in the program again." There was a significant difference for medical student motivation to pursue a career in primary care before (mean, 3.2; SD, 1.1) and after (mean, 3.6; SD, 0.6) participation in the PCMP (t(31), -2.7; $P = .01$). Overall, 27 (84%) mentees also stated that they would participate in the program again.

Of the JABSOM class of 2019 mentees who went through the Spring 2019 Match, 13 (62%) matched into a primary care GME residency specialty: 8 into Family Medicine, 3 into Internal Medicine, and 2 into Pediatrics (Table 3). Seventeen (85%) of the 20 JABSOM class of 2019 mentees completed the post-Match reflection survey. Seven (41%) of these mentees who completed the survey kept in contact with their assigned mentor after they participated in the PCMP. For those mentees who did continue their mentorship relationship after completion of the program, most had additional mentorship meetings during medical school. Overall, 5 (29%) of the 17 JABSOM class of 2019 mentees who completed the survey felt that their participation in the PCMP influenced their choice in GME residency specialty, while 9 (53%) felt that their participation in the program influenced their career choice. All 17 of the JABSOM class of 2019 mentee survey respondents felt that the PCMP is a worthwhile endeavor. Fourteen (82%) of the 17 PCMP mentee survey respondents noted that they would be willing to serve as mentors for first-year medical students upon completing residency. The JABSOM class of 2019 mentee survey respondents also reflected that they "greatly appreciated [their] mentor" and "felt more comfortable talking to my attendings about my aspirations" after participating in the PCMP.

## Discussion

This study found that participation in a 6-month PCMP as a first-year medical student does not correlate with an increased likelihood of matching into a primary care GME residency specialty: 13 (18%) of PCMP participants versus 25 (35%) of non-PCMP participants in the JABSOM class of 2019 entered primary care GME residency specialties. This finding is despite the significant difference for mentee motivation to pursue a career in primary care before and immediately after participation in the PCMP, suggesting a change in the mentees motivation to pursue a primary care career during later years of medical school. This change in career plan throughout medical school is well documented.[4,13] Family Medicine was the only primary care GME specialty that resulted in a greater percentage of students matching into it if they participated in the PCMP (11%) compared to those who did not participate in the PCMP (6%). Although many studies have shown that faculty mentor-

Table 2. JABSOM PCP PCMP Mentee and Mentor Pairings, JABSOM Classes of 2019–2022.

| JABSOM Class | Unable to Pair n (%) | Mentor Specialty | | | Total PCMP Participants n (%) |
|---|---|---|---|---|---|
| | | Family Medicine n (%) | Internal Medicine n (%) | Pediatrics n (%) | |
| 2019 | 1 | 5 | 13 | 3 | 21 |
| 2020 | 6 | 9 | 12 | 3 | 24 |
| 2021 | 6 | 7 | 9 | 5 | 21 |
| 2022 | 0 | 9 | 13 | 4 | 26 |
| Total | 13 (12%)[a] | 30 (33%)[b] | 47 (51%)[b] | 15 (16%)[b] | 92 |

Abbreviations: JABSOM. University of Hawai'i John A. Burns School of Medicine; PCMP, Primary Care Mentorship Program; PCP, Primary Care Progress.
[a] Total number of JABSOM students who applied to participate in the PCMP who were unable to be paired with a community primary care physician divided by the total number of JABSOM students who participated in the PCMP (105).
[b] Total number of JABSOM students who were successfully paired with a community primary care physician, by specialty, divided by the total number of first-year medical students who were successfully paired with a community primary care physician (92).

Table 3. 2019 JABSOM and JABSOM PCP PCMP Prior Mentee GME Residency Match Specialty.

| Primary Care Specialty | PCMP Participants[a] n (%) | Non-PCMP Participants[a] n (%) | JABSOM Total[a] n (%) |
|---|---|---|---|
| Family Medicine | 8 (11%) | 4 (6%) | 12 (17%) |
| Internal Medicine | 3 (4%) | 15 (21%) | 18 (25%) |
| Pediatrics | 2 (3%) | 6 (8%) | 8 (11%) |
| Total | 13 (18%) | 25 (35%) | 38 (53%) |

Abbreviations: JABSOM. University of Hawai'i John A. Burns School of Medicine; GME, general medicine education; PCMP, Primary Care Mentorship Program; PCP, Primary Care Progress.
[a] Number of PCMP versus non-PCMP participants from the JABSOM class of 2019 who matched into a primary care GME residency specialty divided by 72, the total class size of the JABSOM class of 2019.

ship influences medical student specialty choice, this study did not find a correlation between primary care mentorship via participation in a 6-month PCMP and an increased likelihood of entering primary care.[3–7] The structure of the PCMP implemented by Indyk et al at the Einstein College of Medicine that showed an increased likelihood of participants matching into a primary care GME residency specialty, which involved a detailed 3-year PCMP requirement list and a monthly mentor stipend.[8] The reduced length of this study's PCMP, the limited number of requirements of the program, and the lack of direct medical school support of the PCMP likely resulted in a reduced effectiveness of the PCMP in increasing participant matching into primary care. The JABSOM PCMP was structured to not put a significant requirement burden on medical students or busy community primary care physicians to deter them from participating in the program. This structure likely exposes areas of opportunity for improvement for this PCMP compared to the Einstein College of Medicine PCMP. A PCMP supported directly by the medical school itself, with its additional logistical support and ability to hold medical students accountable to meet program requirements, would likely result in a greater number of students entering primary care.

The second goal of this project was to determine if PCMP mentees developed a lasting mentorship relationship with their assigned mentors. For the 7 participants who did continue their mentorship relationship following completion of the PCMP, continued interactions did occur, including additional meetings, clinical experiences, and letters of support for scholarships and residency applications. Based on JABSOM class of 2019 participants stating the PCMP is a worthwhile endeavor 3 years after participation in the program and the number of students who had continued mentorship following completion of the program, it appears the PCMP was a useful program.

The third goal of this study was to determine whether a PCMP is a worthwhile endeavor for medical schools to incorporate into their structured undergraduate medical education curriculum. Based on the overwhelmingly positive qualitative feedback from mentees and that 82% of mentees would participate in the PCMP again, it appears that the implementation of such a program into the structured undergraduate medical education curriculum would be enthusiastically accepted by medical students. A PCMP with greater than 6-month duration and the support of the medical school, such as the program at the Einstein School of Medicine, would likely increase the number of medical students pursuing a career in a primary care GME residency specialty.[8]

## Limitations

Thirteen (12%) of mentee applicants were unable to be paired with a mentor in the PCMP, most likely due to the lack of perceived availability of free time to conduct mentoring by primary care physicians. Soliciting primary care physician associations, such as the Hawai'i Academy of Family Physicians, would have likely resulted in a greater number of mentor volunteers for the PCMP. Only 32 (30%) of PCMP mentees completed the post PCMP feedback survey, likely due to the perceived time needed to meaningfully complete the survey. Mentees and mentors were unable to meet the suggested monthly shadowing experience requirement or outside of clinic communication requirement of the PCMP. As program participation was entirely voluntary for mentees and mentors and not a medical school requirement, the PCMP organizers were not able to enforce the requirements of the program. Mentors, similar to mentees, submitted applications to participate in the PCMP and were surveyed following completion of the PCMP. Unlike the JABSOM class of 2019 mentees, their mentors were not surveyed in 2019 to assess the long-term result of participating in the PCMP for this study. The surveying of mentors who participated in the program would have likely provided meaningful insight into the mentor's perspective on the PCMP, an area of needed study.

## Conclusions

A 6-month PCMP for first-year medical students interested in a career in primary care immediately increases their motivation to pursue a career in primary care upon completion of the program but does not correlate with an increased likelihood of matching into a primary care GME residency specialty. A PCMP does have the potential to create a lasting mentorship relationship through the completion of medical school and overall is a worthwhile endeavor for mentees. Based on the results of other PCMPs, it appears a PCMP directly sponsored by the medical school is more effective at producing medical students matching into primary care GME residency specialties than a PCMP facilitated by an outside organization. A medical school has more resources for logistics, can hold medical students accountable, and can provide compensation to mentors versus an outside organization without these resources, such as PCP. The JABSOM PCP PCMP continues to be successfully implemented by upper-level medical students since its inception in Fall 2015, and based upon these findings, the authors hope that JABSOM, along with other medical schools, will implement a longitudinal PCMP into their undergraduate medical education curriculum. The authors will provide upon request templates for other student-run organizations and medical schools to implement similar programs at their institutions. Every effort to decrease the primary care physician shortage helps our communities, and if a PCMP can increase the number of medical students entering primary care, it should be implemented.

## Conflict of Interest

None of the authors identify a conflict of interest.

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**Appendix 1. Mentor Application.**

1. Name
2. Contact info: email
3. Contact info: phone
4. Specialty area
   a. Internal Medicine
   b. Family Medicine
   c. Pediatrics
   d. Other
5. Mentorship availability
   a. Fall, August - February
   b. Spring, February – July
6. Fellowship training
7. Medical school and graduation year
8. Residency and fellowship
9. Office location
10. Office type
    a. Community health center
    b. Private practice
    c. Group private practice
    d. Kaiser Permanente
    e. Other
11. Quick biography
12. Research Area
13. Agreement to meet program expectations
    a. Yes
    b. No
14. Any additional information you would like to share with the program or your future mentee

**Appendix 2. Community Primary Care Physician Feedback Survey.**

1. Were you able to have a shadowing experience with your mentee? If so, how many times did he/she shadow you?
   a. 0, I did not have a shadowing experience with my mentee
   b. 1 time
   c. 2 times
   d. 3 times
   e. 4 times
   f. 5 times
   g. 6 times
2. Any issues with scheduling shadowing opportunities with your mentee? Any issues encountered on the day(s) your mentee shadowed you? Please provide any additional feedback concerning these shadowing experiences and any ways that you think PCP could improve this experience in the future.
3. One of the program requirements is that you communicated with your mentee at least twice outside of the clinic. Please check all means of communication that apply to your pairing.
   a. E-mail
   b. Phone
   c. Face-to-face
   d. Other
4. The goal of this requirement was to allow your mentee to gain a better understanding of the reality of being a primary care physician. Do you feel you were able to accomplish this? How so? Or why not? Please provide us with any other feedback concerning this requirement.
5. How would you rate your experience in this program?
   a. 1, waste of my time
   b. 2
   c. 3
   d. 4
   e. 5, life-altering
6. Would you serve as a mentor for this program again?
   a. Yes
   b. No
7. Please provide us with any additional feedback regarding your experience with this program! Remember, all responses are anonymous. We are extremely appreciative of any suggestions also!

**Appendix 3. Medical Student Feedback Survey.**

1. Were you able to have a shadowing experience with your mentor? If so, how many times did he/she shadow him/her?
   a. 0, I did not shadow my mentor
   b. 1 time
   c. 2 times
   d. 3 times
   e. 4 times
   f. 5 times
   g. 6 times
2. Any issues with scheduling your shadowing sessions with your mentor? Any issues encountered on the day(s) you shadowed your mentor? Please provide any additional feedback concerning your shadowing experience and any ways that you think PCP could improve this experience in the future.
3. One of the program requirements is that you communicated with your mentor at least twice outside of the clinic. Please check all means of communication that apply to your pairing.
   a. E-mail
   b. Phone
   c. Face-to-face
   d. Other
4. The goal of this requirement was to allow you to gain a better understanding of the reality of being a primary care physician. What were some of the rewards and challenges of primary care you learned? Also, please provide us with any feedback concerning this requirement.
5. How would you rate your experience in this program?
   a. 1, waste of my time
   b. 2
   c. 3
   d. 4
   e. 5, extremely rewarding
6. Before participating in this program, please rate how motivated you were to pursue a career in primary care.
   a. 1, not at all
   b. 2
   c. 3
   d. 4
   e. 5, I am 100% certain I want to be a primary care physician
7. After participating in this program, please rate how motivated you are to pursue a career in primary care.
   a. 1, not at all
   b. 2
   c. 3
   d. 4
   e. 5, I am 100% certain I want to be a primary care physician
8. Would you participate in this program again?
   a. Yes
   b. No
9. Please provide us with any additional feedback regarding your experience with this program! Remember, all responses are anonymous.

**Appendix 4. Fourth year medical student reflection survey.**

1. What is your name?
2. During which semester/year did you participate in the mentorship program?
3. Who was your assigned mentor through the Primary Care Mentorship Program?
4. Into what specialty did you match?
   a. Family Medicine
   b. Internal Medicine
   c. Pediatrics
   d. Other
5. Did you keep in contact with your mentor after your assigned mentorship period?
   a. Yes
   b. No
   c. Other
6. If so, in what way did you continue your mentorship relationship following the assigned mentorship period? (Check all that apply or fill in other with additional items he/she helped with)
   a. MS3 6L Assigned Preceptor
   b. Additional MS1/MS2/MS3/MS4 Mentorship Meetings (in person or via email/phone)
   c. Residency Application Letter of Recommendation Writer
   d. Scholarship/Other Application Letter of Recommendation Writer
   e. MS4 Preceptorship
   f. Other
7. Do you feel that your participation in the Primary Care Mentorship Program affected your choice in residency program?
   a. Yes
   b. No
   c. Other
8. Do you feel that your participation in the Primary Care Mentorship Program affected your choice in career?
   a. Yes
   b. No
   c. Other
9. Do you think the Primary Care Mentorship Program is a worthwhile endeavor for our organization, based on your participation in our program?
   a. Yes
   b. No
   c. Other
10. Based on your experience in the Primary Care Mentorship Program, at this point, would you serve as a mentor for MS1s interested in primary care once you complete residency?
    a. Yes
    b. No
    c. Other
11. Do you have any meaningful reflections on your experience in the Primary Care Mentorship Program that you would like to share with the us?

# Assessing the Status of Diabetes Associations in the Pacific: A Starting Point for Strengthening Associations to Manage Diabetes

Si Thu Win Tin PhD; Elisiva Na'ati MDiet; Solene Bertrand MES; Karen Fukofuka PGDPH; Paula Vivili MPH; Sunia Soakai MBA; Viliami Puloka MPH; and Erin Passmore DrPH

## Abstract

*This study aimed to assess the status of national diabetes associations in the Pacific Island Countries and Territories as a starting point for strengthening their development and effectiveness in the prevention and control of diabetes. This cross-sectional study was conducted in 21 Pacific Island Countries and Territories using a structured questionnaire that gathered information from national non-communicable diseases prevention and control focal persons on diabetes associations, organizational structure, funding sources, and ongoing activities to address diabetes. The overall status of national diabetes associations was assessed using standardized criteria. Of the 21 countries surveyed, 18 (86%) responded. Of these, 12 (67%; American Samoa, Northern Mariana Islands, Federated States of Micronesia, French Polynesia, Fiji, Guam, Nauru, Papua New Guinea, Marshall Islands, Solomon Islands, Tonga, and Vanuatu) have a national diabetes association. Half of the existing associations are fully functioning, while the remainder is either partially functioning or not functioning. Only 50% of existing associations have a regular funding source, and many lack clear visions and workable governance structures. This study fills a knowledge gap on the current status of associations and forms a baseline from which associations can be strengthened. It also draws attention to the need for Pacific leaders to invest and engage more in civil societies for better and effective diabetes care for all.*

## Keywords

*Association, diabetes, non-communicable diseases, Pacific Islands Countries and Territories*

## Abbreviations

*NCD = non-communicable diseases*
*PICTs = Pacific Island Countries and Territories*
*SPC = The Pacific Community*

## Introduction

Diabetes imposes a high economic cost and is a major health and development challenge globally.[1,2] Premature deaths and disability from diabetes are creating a socioeconomic crisis that challenges global progress to achieve the World Health Organization's Sustainable Development Goal 3 "ensure healthy lives and promote well-being for all at all ages," particularly Target 3.4, "reduce by one third premature mortality from non-communicable diseases (NCDs) by 2030."[3]

The prevalence of diabetes in Pacific Islands Countries and Territories (PICTs)—American Samoa, Common Wealth of the Northern Mariana Islands, Cook Islands, Fiji, Federated States of Micronesia, French Polynesia, Guam, Kiribati, Marshall Islands, Niue, New Caledonia, Nauru, Papua New Guinea, Palau, Samoa, Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu, and Wallis and Futuna —are among the highest in the world. For example, in 2018, 45.4% of adults in American Samoa[4] and 29.4% in the Kosrae-Federated States of Micronesia[5] have diabetes, which was much higher than the estimated global prevalence of 9% in 2019.[6] Diabetes-related complications in PICTs are also substantial; in 2013, the prevalence of amputations and diabetic retinopathies are approximately 11% and 69% respectively among people with diabetes in some PICTs.[7] Cost for diabetes is enormous. For example, in Nauru and the Solomon Islands, diabetes care consumed 20% of annual government health care expenditure in 2007 and 2011, respectively.[8] These estimates were much higher than the global average of 12% in 2019.[6]

Declarations and commitments aimed at addressing diabetes and other NCD consistently highlight the urgent need for a whole-of-government and whole-of-society approach.[9,10] It is well-recognized that stakeholders, such as diabetes associations, play an important role in tackling diabetes. However, limited information is available about the existence, establishment, structure, governance, management, activities, and effectiveness of Pacific diabetes associations. Therefore, this study aimed to assess the status of diabetes associations in PICTs as a starting point for strengthening their development and effectiveness in the prevention and control of diabetes. The findings of this survey will help identify the support needs to strengthen the function of diabetes associations, and ultimately to contribute to achieving the Healthy Island Vision—a unifying theme endorsed by the Pacific Health Ministers to guide health development in the Pacific region—particularly the vision on "people work and age with dignity by reducing avoidable disease burden and premature deaths due to NCD".[11]

## Methods

This cross-sectional study was conducted in all 21 PICTs across the Pacific region to identify the existence and assess the status of their national diabetes associations. A structured self-administered questionnaire was developed by the NCD policy experts within the public health division of the Pacific Community (SPC), and contents were validated by the selective

PICTs' NCD prevention and control focal persons. The national NCD focal persons designated by their respective Ministries of Health were selected to complete the survey, given that the national NCD focal persons support and oversee the function of national diabetes associations. The self-administered questionnaire was distributed electronically via email to the national NCD focal persons of all 21 PICTs across the Pacific. If there was no initial response, follow-up by email was conducted to complete questionnaires, with initial data collection occurring between June 2017 and August 2017. The answers in the completed questionnaires were crossed-checked by the SPC's NCD policy experts and PICTs' national NCD focal persons and representatives from diabetes associations who attended the inaugural Pacific diabetes association meeting in September 2017. An additional period of email follow-up was conducted with national NCD focal persons between September 2017 and January 2018 to clarify any key points. The questionnaire sought information on the existence of diabetes associations, organizational structure, funding sources, and ongoing activities to address diabetes. One open-ended question on the questionnaire also sought to identify the support needs for their diabetes associations to function effectively.

The data were compiled and analyzed using Microsoft Office Excel 2016 issued by DigiCert in Lehi, USA. Where relevant, data were reported as numbers and percentages. The overall status of diabetes associations was assessed. Associations were categorized as "well-functioning" if they met the following 3 criteria: (1) has a formal organizational structure, (2) has a regular source of funding, and (3) is implementing 3 or more ongoing diabetes prevention and control activities. Associations meeting 1 or 2 of these criteria were categorized as "partially functioning." Associations meeting none of these criteria were categorized as "not functioning." The categories of assessment for overall functioning status were determined by the Pacific Community's (SPC) NCD policy experts. This study was conducted with approval from SPC's Scientific and Technical Expert Group.

## Results

Of the 21 PICTs surveyed, 18 responded (Table 1). The response rate is 86%. Of the 18 countries that responded to the survey, 12 (67%) have a national diabetes association, and 5 of these (Fiji, Nauru, Papua New Guinea, Tonga, and Vanuatu) are International Diabetes Federation member associations. The Cook Islands do not currently have a diabetes association; however, they plan to establish one in the next 12 months. The remaining 5 PICTs (Kiribati, Niue, Palau, Tokelau, and Wallis and Futuna) do not have a diabetes association and do not plan to establish one in the next 12 months. Some associations have been established for over 20 years (eg, French Polynesia; Table 2).

Table 1. Pacific Island Countries and Territories that Responded to the National Diabetes Association Questionnaire

| Description | n (%) (N=21) | Name of Country |
|---|---|---|
| Countries responded | 18 (86%) | American Samoa, Commonwealth of the Northern Mariana Islands, Cook Islands, FSM, French Polynesia, Fiji, Guam, Kiribati, Nauru, Niue, Papua New Guinea, Palau, Marshall Islands, Solomon Islands, Tokelau, Tonga, Vanuatu, Wallis and Futuna |

Table 2. Existence of National Diabetes Associations in Pacific Island Countries and Territories

| Description | n (%) (N=18) | Name of Country (Year of Establishment)[a] |
|---|---|---|
| Of the countries responded, countries with a diabetes association | 12 (67%) | American Samoa (2013), Commonwealth of the Northern Mariana Islands (2002), Federated States of Micronesia (2010), French Polynesia (1990), Fiji (2012), Guam (2008), Nauru (2008), Papua New Guinea (1996), Marshall Islands (2010), Solomon Islands (2000), Tonga (2000), Vanuatu (2007) |
| Of the countries responded, countries which do not currently have a diabetes association, however, plan to establish 1 in the next 12 months | 1 (5%) | Cook Islands |
| Of the countries responded, countries which do not currently have a diabetes association and do not plan to establish 1 in the next 12 months | 5 (28%) | Kiribati, Niue, Palau, Tokelau, Wallis and Futuna |

[a] The year a national diabetes association was first established in the Pacific Island Country or Territory.

Table 3 shows the statuses of existing diabetes associations regarding organizational structure, funding source, and ongoing diabetes prevention and control activities. Seven (58%) associations have established and functioning organizational structures with a specific purpose, vision and goal, and board of directors or committee for governance. Half of the existing associations have regular funding sources. The majority of the existing associations hold annual events to commemorate international days (eg, World Diabetes Day, World Health Day) and reported that they work closely with other government organizations, including the Ministries of Health in their respective countries.

The overall functioning status of the associations was assessed. Of the 12 existing associations that responded to the survey, 6 (50%) associations (American Samoa, Fiji, Federated States of Micronesia, French Polynesia, Guam, and Marshall Islands) are reported to be functioning well but need further strengthening, 3 (25%) associations (Commonwealth of the Northern Mariana Islands, Papua New Guinea, and Tonga) are partially functioning, and 3 (25%) associations (Nauru, Solomon Islands, and Vanuatu) are not functioning and need reactivation.

Respondents were also asked to identify what support was required for their diabetes association to function effectively. Support needs identified by respondents included the need for developing organization structure, training for NCD and associated risk factors, funding to support interventions, and reactivating defunct associations. Other support needs mentioned were providing health promotion resources, information sharing, and developing a diabetes registry (Table 4).

Table 3. Status of Existing Diabetes Associations in Pacific Island Countries and Territories

| Description | n (%) (N=12) | Name of Country |
|---|---|---|
| **Organization** | | |
| Functioning diabetes associations with a specific purpose, a vision and goal, and a board of directors/ committee for governance | 7 (58%) | American Samoa, Federated States of Micronesia, French Polynesia, Fiji, Guam, Marshall Islands, Tonga |
| **Funding** | | |
| Diabetes associations with a regular source of funding (eg, donor agencies) | 6 (50%) | American Samoa, Federated States of Micronesia, French Polynesia, Fiji, Guam, Marshall Islands |
| **Activities** | | |
| Diabetes associations that host annual events (eg, World Diabetes Day, World Food Day, World Health Day) | 9 (75%) | American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, French Polynesia, Fiji, Guam, Marshall Islands, Papua New Guinea, Tonga |
| Diabetes associations that organize education and awareness activities on an ongoing basis | 7 (58%) | American Samoa, Federated States of Micronesia, French Polynesia, Fiji, Guam, Marshall Islands, Papua New Guinea |
| Diabetes associations that organize ongoing health programs (eg, physical activity program, health food cooking demonstration program) | 4 (33%) | Federated States of Micronesia, Fiji, Guam, Marshall Islands |
| Diabetes associations that produce resources (eg, pamphlets, flyers, posters) | 4 (33%) | Federated States of Micronesia, Fiji, Guam, Marshall Islands |
| Diabetes associations that collaborate with other organizations in their country (eg, Ministries of Health, schools, colleges, non-government organizations) | 9 (75%) | American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, French Polynesia, Fiji, Guam, Marshall Islands, Papua New Guinea, Tonga |

| Table 4. Support Needs Identified by the Existing Diabetes Associations in Pacific Island Countries and Territories | | |
|---|---|---|
| **Description** | **n (%) (N=12)** | **Name of Country** |
| Developing organization structure | 4 (33%) | Nauru, Papua New Guinea, Solomon Islands, Vanuatu |
| Training about non-communicable diseases and associated risk factors | 9 (75%) | American Samoa, Federated States of Micronesia, French Polynesia, Fiji, Guam, Marshall Islands, Nauru, Papua New Guinea, Tonga |
| Funding to support interventions | 5 (42%) | Nauru, Papua New Guinea, Solomon Islands, Vanuatu, Tonga |
| Reactivation of associations | 3 (25%) | Nauru, Papua New Guinea, Solomon Islands, Vanuatu |
| Other (eg, providing health promotion resources, information sharing, developing diabetes registry) | 3 (25%) | Guam, Fiji, Solomon Islands |

## Discussion

This study provides information on the status of diabetes associations in PICTs and identifies areas that need to be enhanced to scale up their efforts in combating diabetes. A diverse range of diabetes prevention and care activities were supported by existing associations, including hosting annual events, running health programs, and producing information resources about diabetes.

There are very limited studies examining the existence and status of diabetes associations in PICTs, which are relevant to make comparisons with the findings of this study. However, there are examples of established and sustained robust diabetes associations that can speak up for the needs and rights of people with diabetes, such as Diabetes Australia.[12] However, this study identifies that only half of the Pacific diabetes associations that responded to the survey are fully functioning—the remainder are either partially functioning (n=3, 25%) or not functioning at all (n=3, 25%). Some associations faced organizational challenges, including that only half of associations have a regular funding source, and many do not have a robust governance structure or specific purpose and vision. This finding demonstrates the need to establish and strengthen diabetes associations in implementing acceptable practices to address diabetes effectively.

Capacity and resources to address diabetes and the effectiveness and sustainability of these diabetes associations are of major concern. Only 4 (33%) of associations reported that they produce health promotion resources (eg, pamphlets and flyers) and organize ongoing health programs addressing NCD risk factors (eg, physical activity promotion program and healthy food cooking demonstration program). Given that funding and capacity building through training were identified as support needs by most associations, it is critical for PICT governments and development agencies to invest more in strengthening diabetes associations to scale up diabetes prevention and control actions at the national level.

Given PICTs have some of the highest rates of diabetes in the world. Diabetes has become a major health and development challenge in the Pacific region. There have been several declarations and commitments aimed at addressing diabetes as a whole-of-government and whole-of-society approach. For example, the Pacific NCD roadmap[13] endorsed by Pacific leaders in 2014 recognized the need for multi-stakeholder involvement to address NCD, a commitment reaffirmed by Pacific leaders at the 2016 Pacific NCD Summit[10] and Pacific Health Ministers Meeting 2019.[14] However, there have been challenges to ensuring the response is a collaborative approach involving stakeholders including diabetes associations. These challenges include limited capacity, resource constraints, and competing priorities of stakeholders in PICTs.

Recognizing these challenges and considering the preliminary findings of this study, SPC conducted an inaugural regional meeting of Pacific diabetes associations in September 2017 in Fiji. The meeting aimed to strengthen Pacific diabetes associations and enhance collaboration to address the diabetes epidemic. The meeting was attended by representatives from 12 PICTs (American Samoa, Cook Islands, Fiji, Federated States of Micronesia, French Polynesia, Guam, Marshall Islands, Nauru, Papua New Guinea, Solomon Islands, Tonga, and Vanuatu), and development partners and stakeholders, including the World Health Organization, United Nations agencies, Fred Hollows Foundation New Zealand, Diabetes Australia, Diabetes New Zealand, and academic institutions.

Preliminary data presented at this meeting helped generate a common understanding among diabetes associations on actions needed to improve the function of their associations, the prerequisites to sustain their associations, and resources and opportunities to strengthen in-country and regional collaboration to foster their growth and development. This meeting also increased awareness, knowledge, and understanding of the role and influence of associations in addressing diabetes at the national and regional levels. More importantly, considering the

preliminary findings of this study, the participants developed an 'action plan' for their national diabetes association and identified future focus areas and collaborative initiatives. Following this meeting, SPC has continued to support diabetes associations to ensure associations are robust and well-functioning.

From 2018 to 2019, several important actions have been observed at the country level. For example, the Solomon Islands and Nauru have committed to reactivating their existing national diabetes associations. Fiji, Tonga, Marshall Islands, and Guam have further strengthened their association by implementing diabetes prevention and care activities in their respective countries. A follow-up study replicating the process of the current study should be considered to monitor the progress on the status of associations.

This study fills a significant knowledge gap by providing an overview of the status of associations and forms a baseline from which associations can be strengthened. More importantly, it draws attention to the need for Pacific leaders to focus and invest more in engaging and mobilizing civil societies in tackling diabetes more effectively. PICTs should be encouraged to continue to strengthen their diabetes associations, and PICTs which do not have existing diabetes associations should be encouraged to establish one, to strengthen their efforts in addressing evidence-based cost-effective diabetes intervention in a whole-of-society approach. However, this study has a limitation that needs to be improved in the future follow-up study. For example, given that SPC's NCD policy experts solely determined the categories of assessment for overall functioning status, it may not adequately reflect the actual functioning status of the associations. Despite the limitation, the categories on functioning status are necessary to prioritize which associations need the most support from the development partners in the Pacific to enhance their efforts in prevention and control of diabetes.

In conclusion, mounting a sustainable response to the diabetes epidemic is an urgent priority. It is imperative to assess and understand the status of key stakeholders, such as diabetes associations. Engaging diabetes associations by design and not by default is key in our collaborative approach to address diabetes in the Pacific. Our shared vision of the Healthy Islands, particularly the vision on "people work and age with dignity" [11] through efforts to reduce avoidable disease burden and premature deaths due to NCD, will be realized when diabetes associations are sustained and no one left behind. These efforts will ensure Pacific people reach their potential and lead healthy lives.

## Conflict of Interest

None of the authors identify a conflict of interest.


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# Hawai‘i Journal of Health & Social Welfare (HJH&SW)

## Style Guide for the Use of Native Hawaiian Words and Diacritical Markings

The HJH&SW encourages authors to use the appropriate diacritical markings (the ‘okina and the kahakō) for all Hawaiian words. We recommend verifying words with the Hawaiian Language Dictionary (http://www.wehewehe.org/) or with the University of Hawai‘i Hawaiian Language Online (http://www.hawaii.edu/site/info/diacritics.php).

Authors should also note that Hawaiian refers to people of Native Hawaiian descent. People who live in Hawai‘i are referred to as Hawai‘i residents.

Hawaiian words that are not proper nouns (such as *keiki* and *kūpuna*) should be written in italics throughout the manuscript, and a definition should be provided in parentheses the first time the word is used in the manuscript.

Examples of Hawaiian words that may appear in the HJH&SW:

| | |
|---|---|
| ***‘āina*** | ***Mānoa*** |
| ***ali‘i*** | ***Māori*** |
| ***Hawai‘i*** | ***Moloka‘i*** |
| ***kūpuna*** | ***O‘ahu*** |
| ***Kaua‘i*** | ***‘ohana*** |
| ***Lāna‘i*** | ***Wai‘anae*** |

# Hawai'i Journal of Health & Social Welfare (HJH&SW)

## Guidelines for Publication of HJH&SW Supplements

The Hawai'i Journal of Health & Social Welfare (HJH&SW) partners with organizations, university divisions, and other research units to produce topic-specific issues of the journal known as supplements. Supplements must have educational value, be useful to HJH&SW readers, and contain data not previously published elsewhere. Each supplement must have a sponsor(s) who will work with the HJH&SW staff to coordinate all steps of the process. Please contact the editors at hjhsw@hawaii.edu for more information if you would like to pursue creating a supplement.

The following are general guidelines for publication of supplements:

1. Organizations, university divisions, and other research units considering publication of a sponsored supplement should consult with the HJH&SW editorial staff to make certain the educational objectives and value of the supplement are optimized during the planning process.

2. Supplements should treat broad topics in an impartial and unbiased manner. They must have educational value, be useful to HJH&SW readership, and contain data not previously published elsewhere.

3. Supplements must have a sponsor who will act as the guest editor of the supplement. The sponsor will be responsible for every step of the publication process including development of the theme/concept, peer review, editing, preliminary copy editing (ie, proof reading and first round of copy editing), and marketing of the publication. HJH&SW staff will only be involved in layout, final copy editing and reviewing final proofs. It is important that the sponsor is aware of all steps to publication. The sponsor will:

a. Be the point of contact with HJH&SW for all issues pertaining to the supplement.
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d. Ensure that all articles adhere to the guidelines set forth in journal's Instructions to Authors page, especially the instructions for manuscript preparation and the statistical guidelines.
e. Obtain a signed Copyright Transfer Agreement for each article from all authors.
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g. Work with the editorial staff to create and adhere to a timeline for the publication of the supplement.
h. Communicate any issues or desired changes to the HJH&SW staff in a timely manner.

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- Final date to submit a list of all articles, with working titles and authors
- Final date for submitting Word documents for copy editing
- Final date for submitting Word documents for layout
- Final date to request changes to page proofs (Please note that changes to page proofs will be made only to fix any errors that were introduced during layout. Other editing changes will incur an additional fee of $50 per page.)

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9. The editorial board reserves the right of final review and approval of all supplement contents. The HJH&SW will maintain the copyright of all journal contents.

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**Sample Workflow and Timeline for a Supplement**

1. The sponsor contacts the HJH&SW editors (hjhsw@hawaii.edu) to discuss the supplement topic, estimated timeline, length and cost. HJH&SW staff will review the journal requirements for articles and share our review process with the sponsor. **Time frame: 2 weeks**

2. The sponsor will complete the draft contract and pay a non-refundable deposit of $2500 or half the contract value. **Time frame: 3 days**

3. The sponsor will solicit articles for the supplement. **Time frame: 3-6 months**

Articles must comply with:

- Instructions for Manuscript Preparation and Submission of Research Articles
- Instructions for Manuscript Preparation and Submission of Columns
- HJH&SW Statistical Guidelines
- HJH&SW Style Guide for Native Hawaiian Words and Phrases
  AMA Manual of Style A free summary can be found here.

4. The sponsor will oversee the article selection, peer review, and editing process. We recommend that time be allowed for at least two rounds of reviews for each article. **Time frame: 3-6 months**

- Ensure that each article includes Institutional Review Board (IRB) review and approval, and a statement disclosing any conflicts of interest.
- Obtain a Copyright Transfer Agreement signed by all authors for each article.

5. *Optional*: During this time, the sponsor can solicit advertisements for the supplement to help defray costs for publication and/or printing. To initiate this process, the sponsor will work the HJH&SW advertising representative Michael Roth at 808-595-4124 or roth-comm@gmail.com.

6. The sponsor or their designee will conduct a final review of each article to ensure adherence to HJH&SW guidelines and AMA style. **Time frame: 2 weeks**

7. For each article, the sponsor will submit the final Word document and Copyright Transfer Agreement to the HJH&SW journal production editor. The journal production editor will send the articles to the copy editor for final journal style review. Copyediting will be 8 hours per edition plus 1 hour per article for additional articles purchased. Any additional hours will be billed at $100 per hour. **Time frame: 2 weeks**

8. The sponsor will submit the final articles to the layout editor for formatting. **Time frame: 1 month**
Acting in the role of guest editor, the sponsor will include a column introducing the supplement.
**IMPORTANT:** All articles submitted for layout should be in their finalized form. Page proofs will be returned to the sponsor for their review and approval, but changes will only be made to fix any errors that were introduced during the layout process. Any editing or changes to the text or figures after the initial copy layout will incur a fee of $50 per page.

9. The sponsor will review the electronic copy from the layout editor and submit any final corrections. **Time frame: 5 working days**

10. The layout editor will make the final corrections and provide a finished electronic copy of the supplement to the sponsoring editors to allow time for printing.

11. The managing editor will work with the sponsor to draft a press release. Sponsors should contact the managing editor at least 30 days prior to the date of publication to plan and script the press release. Sponsors are encouraged to submit 1-2 photos to accompany the press release. Note that obtaining signed photo releases is the responsibility of the sponsor.

12. The supplement will be published online along with the press release. An electronic copy will be sent to our subscribers and circulation lists, and the edition will be forwarded to the National Library of Medicine for indexing and made available for no cost access to the public.

Revised 2/6/20

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