How ACE2 Affect Symptoms of COVID-19

By: Kathryn Rivas

Intro

We all have the Angiotensin I converting gene (ACE) which provides instruction for making the Angiotensin-converting enzyme (ACE2). ACE2 is ubiquitous to the human body, but it is primarily expressed near the lung, heart, intestine, blood vessel, nose and mouth. The ACE gene allows the ACE2 enzyme to cut up proteins called Angiotensin I. By cutting up this protein the enzyme converts it to Angiotensin II (ANGII). ANGII increases blood pressure, cell growth, and inflames blood vessels. The ACE2 enzyme generates Almandine and Angiotensin (1-7) from ANGII. These two peptides help lower blood pressure and stop inflammation in blood vessels by regulating ANGII.

Intro continued…

Within ACE there is a gene variant called the I/D (Insertion/Deletion) variant which produces 3 genotypes: II, DI, and DD. These differ among individuals because each genotype influences how much of the ACE enzyme the body produces. ACE2 acts as a receptor for SARS-CoV-2 as the virus is a spiked protein and it will be able to latch onto ACE2. This attachment initiates entry into the cells to become infected with SARS-CoV-2.When SARS-CoV-2 is bound to the ACE2 receptor, it prevents ACE2 from regulating ANGII. This allows ANGII to injure tissue and contribute to the lung and heart injuries that COVID-19 patients usually have.Since everyone has the ACE gene, but different genotypes of the I/D allele, people are unsure why they experience different symptoms when they have COVID. Do different various ACE2 genotypes cause different symptoms?

Hypothesis

If we are able to test people's' DNA, who have had COVID-19 in the past, then we will see a pattern with how their symptoms affected them in relation to their ACE-2 genotypes. We will then be able to identify which people will have what specific symptom based on their genotype due to the data that was collected.

Procedure

Participants DNA in amplification tubes before putting into a PCR
Taken By Kathryn Rivas

Part A: Preparation

1) Make a survey based on participants experience with COVID-19.
2) Collect salt water and insert less than 2 ml into 15ml Conical centrifuge tube.

Part B: Beginning Experimentation

1) Hand out survey to participants
2) After completing survey ask participants to swish salt water in their mouth for 1 minute to spit into a dixie cup.
3) Transfer dixie cup into the15ml Conical centrifuge tube.
4) Label each tube a number corresponding to participants survey.

Procedure

Part C: Extraction and Isolation

1) Test samples in a BSL-2 Lab:
2) Extract DNA from 15ml Conical centrifuge tubes using a pipette set to 1300 µl to eppy
3) Centrifuge samples at 13400 RPM (revolutions per minute) for 90 seconds
4) Take 800 µl of liquid off of the top of the tube
5) Take 700 µl of PBS and invert tubes
6) Remove supernatant to leave approximately 100 µl of liquid
7) Resuspend cell pellet using vortex
8) Load 150 µl chelex into samples
9) Incubate samples at 56℃ for 20 minutes
10) Place samples into boiling water for 5 minutes
11) Remove 3.5 µl of DNA into an amplification tube
12) Add 21.5 µl of ACE2 primer onto the side of the amplification tube to amplify ACE2 gene.
13) Load into PCR and wait until timer is done

Photo of Kathryn Rivas loading DNA samples into Conical Centrifuge tubes
Taken by Amy Stark

Photo of Kathryn Rivas holding DNA samples
Taken by Amy Stark

Procedure

Part D: End of Experimentation

1) Add .9 µl of glow stain dye into each sample
2) Cover samples with foil and wait 5-15 minutes
3) While waiting, set up gel electrophoresis:
4) Prepare agarose gel in casting tray
5) Fill up tray using a TBE buffer
6) Submerge gel under buffer in electrophoresis chamber
7) Uncover foil and add 3 µl of loading dye into DNA samples
8) Mix dyes by pipetting up and down gently if not fully mixed (should be green)
9) Load 7.5 µl into each well
10) Connect electrodes and apply 130 volts for 30 minutes
11) Move gel onto UV transilluminator
12) View genotypes of the different samples with a UV light
13) Record data

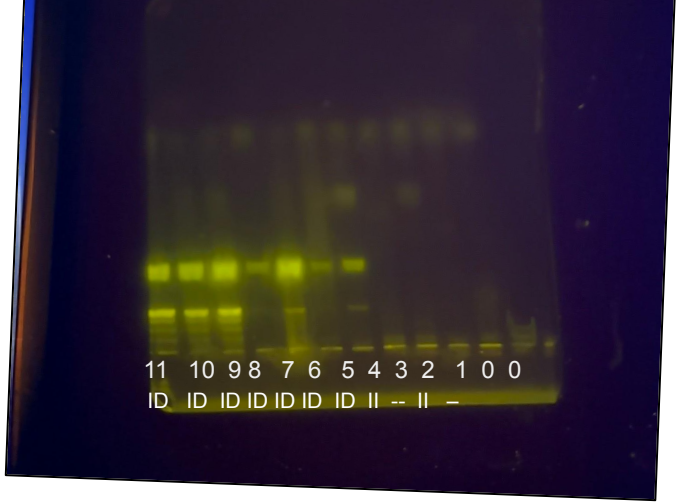


Photo of participants #1-#11 genotypes after gel electrophoresis under a UV transilluminator. Taken by Kathryn Rivas

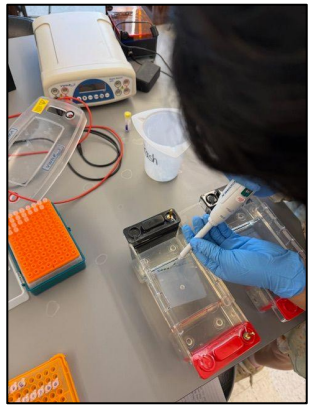
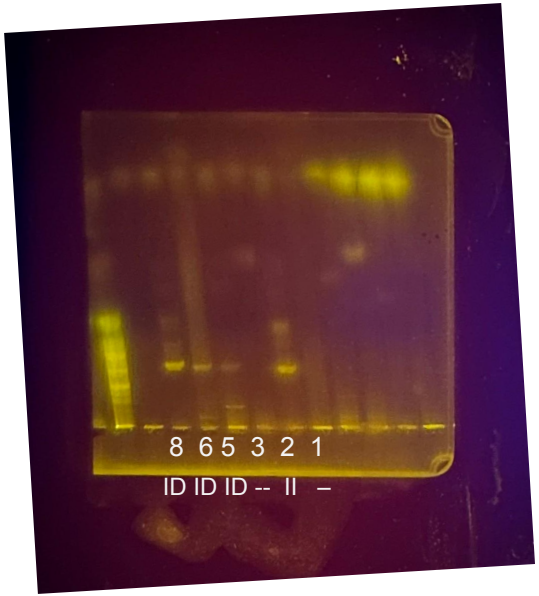
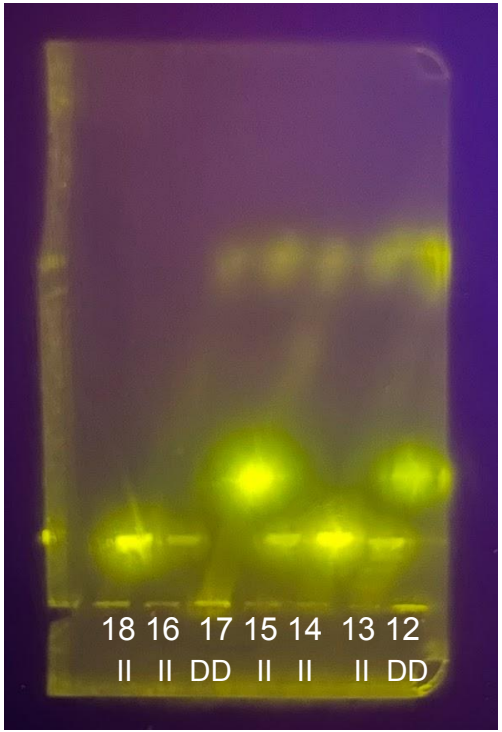


Photo of Kathryn Rivas loading mixed dyes into wells of gel. Taken by Amy Stark



Verification samples of participants #1-#4,6,8, 12 to ensure ID genotype. Taken by Kathryn Rivas



Participants #12-18 genotypes
Taken by Kathryn Rivas

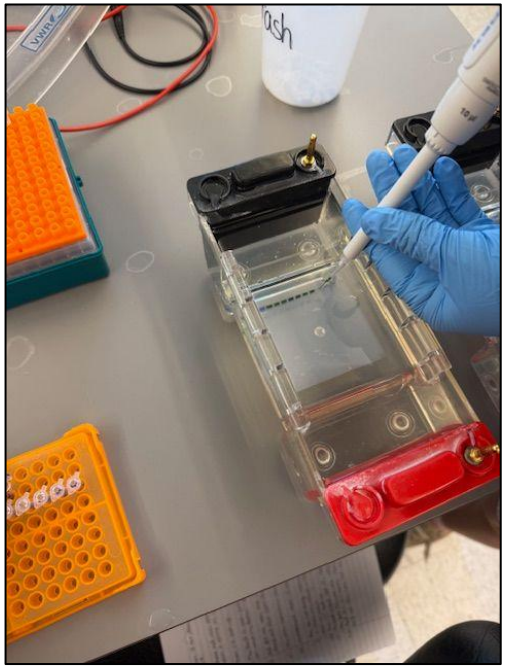
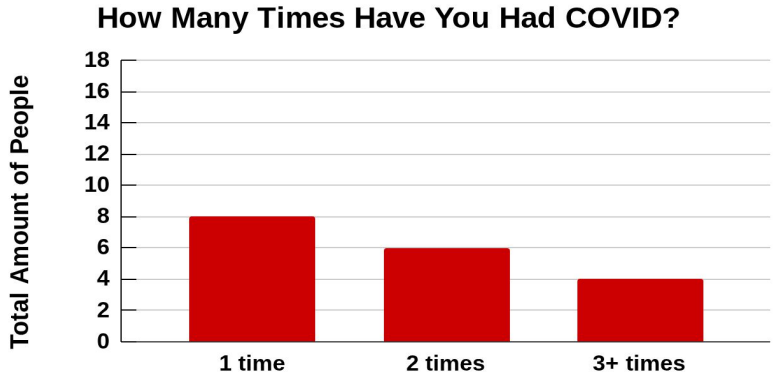
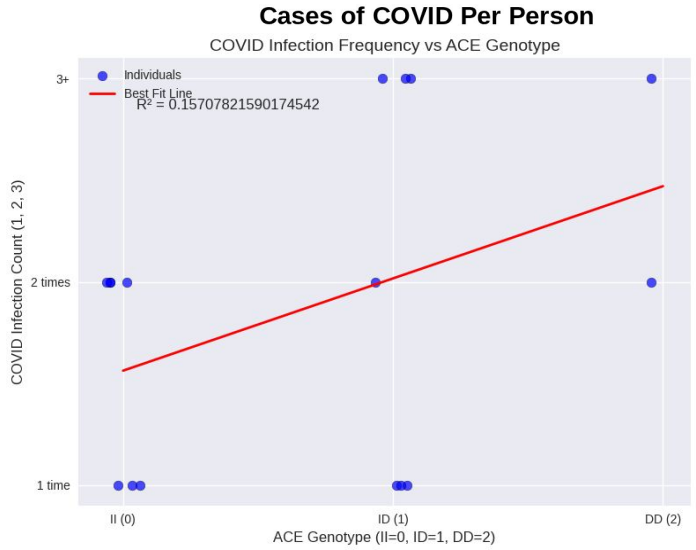


Photo of Kathryn Rivas loading mixed dyes into wells of gel. Taken by Amy Stark

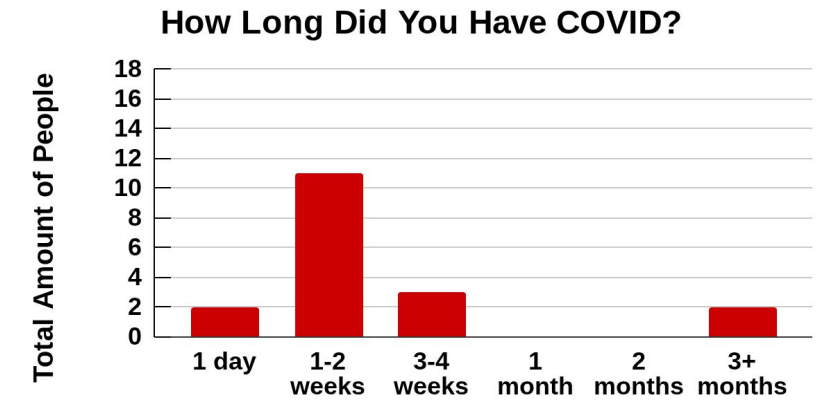
Data Tables of How Many Times Participants Have Had COVID

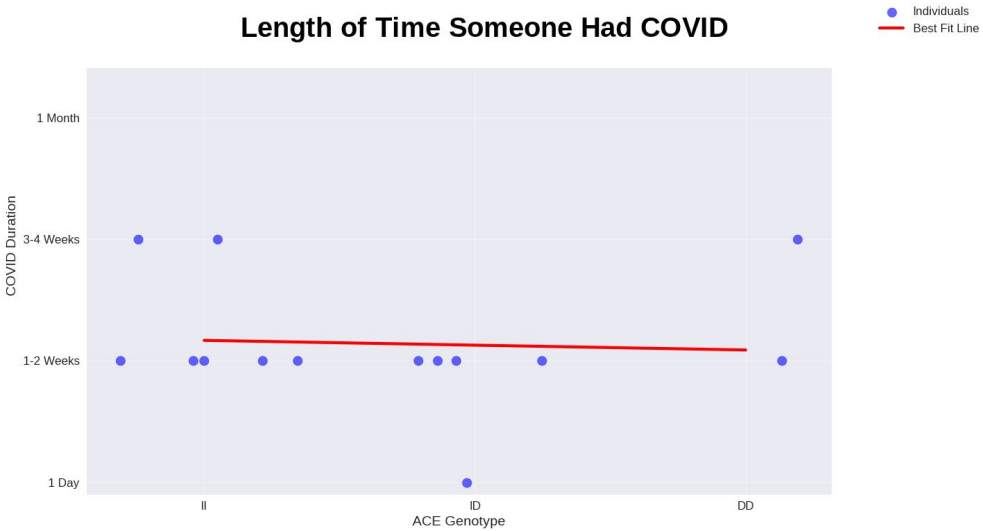




Genotype	Patient #	# of times they've had COVID
—	1	1
—	3	1
II	2	2
II	4	2
II	15	2
II	13	1
II	14	1
II	16	1
II	18	1
ID	6	3+
ID	7	3+
ID	10	3+
ID	5	1
ID	8	1
ID	11	1
ID	9	2
DD	12	3+
DD	17	2

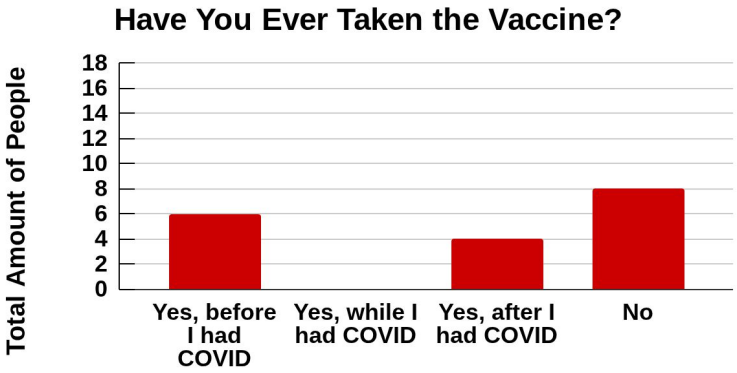
Participants Duration of Having COVID

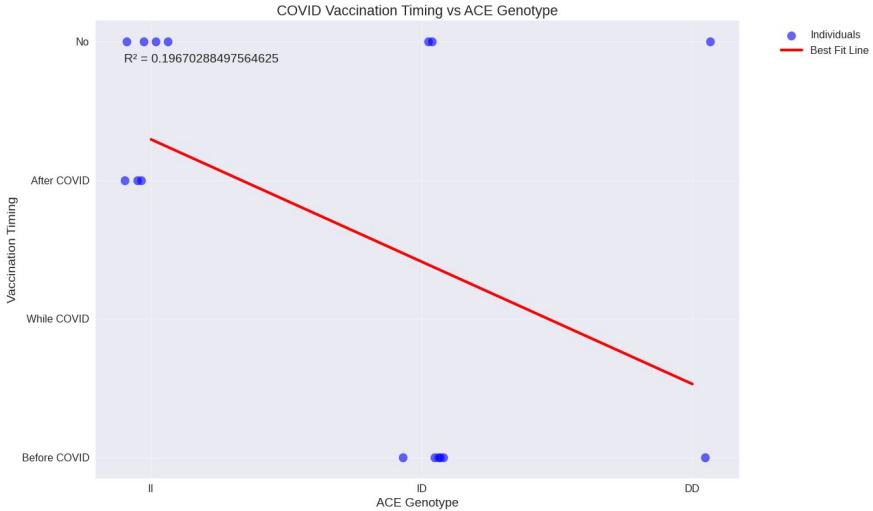




Genotype	Patient #	Duration of having COVID
—	1	1-2 Weeks
—	3	1 day
II	2	1-2 Weeks
II	4	1-2 Weeks
II	13	3-4 Weeks
II	15	3-4 Weeks
II	14	1-2 Weeks
II	16	1-2 Weeks
II	18	1-2 Weeks
ID	5	1 day
ID	6	1-2 Weeks
ID	7	3+ Months
ID	8	1-2 Weeks
ID	9	3+ Months
ID	10	1-2 Weeks
ID	11	1-2 Weeks
DD	12	1-2 Weeks
DD	17	3-4 Weeks

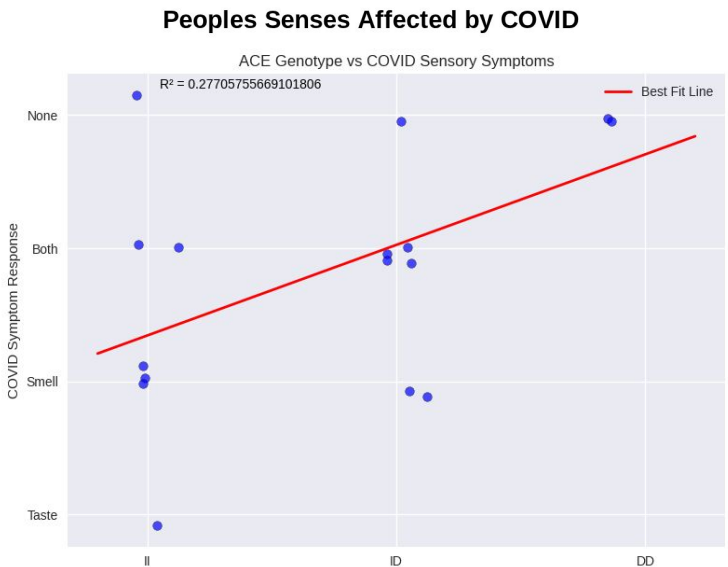
Participants Who Took the Vaccine





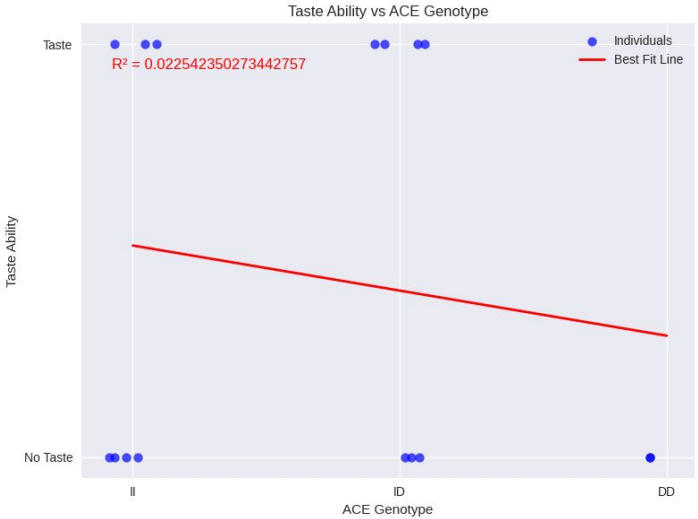
Genotype	Patient #	Responses to Taking the Vaccine
—	1	Yes, after having COVID
—	3	No
II	2	No
II	4	No
II	13	Yes, after having COVID
II	15	No
II	14	No
II	16	Yes, after having COVID
II	18	Yes, after having COVID
ID	5	No
ID	6	Yes, before having COVID
ID	7	Yes, before having COVID
ID	8	No
ID	9	Yes, before having COVID
ID	10	Yes, before having COVID
ID	11	Yes, before having COVID
DD	12	Yes, before having COVID
DD	17	No

Participants Who Lost Their Sense of Taste or Smell



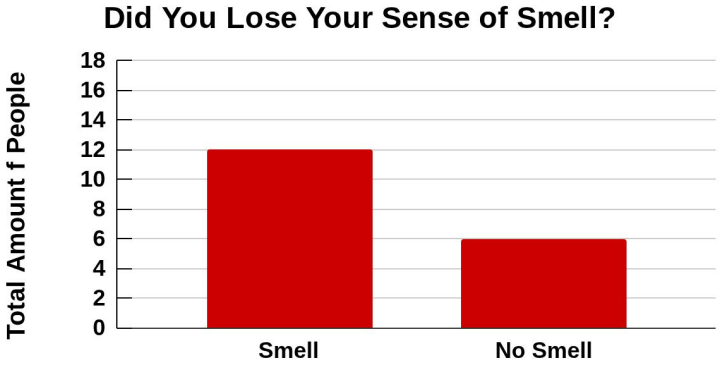
Genotype	Patient #	Senses Affected: Taste or Smell
—	1	Both
—	3	None
II	2	Smell
II	4	Both
II	13	Both
II	15	Smell
II	14	Taste
II	16	Smell
II	18	None
ID	5	None
ID	6	Smell
ID	7	Smell
ID	8	Both
ID	9	Both
ID	10	Both
ID	11	Both
DD	12	None
DD	17	None

Participants Who Lost Their Sense of Taste

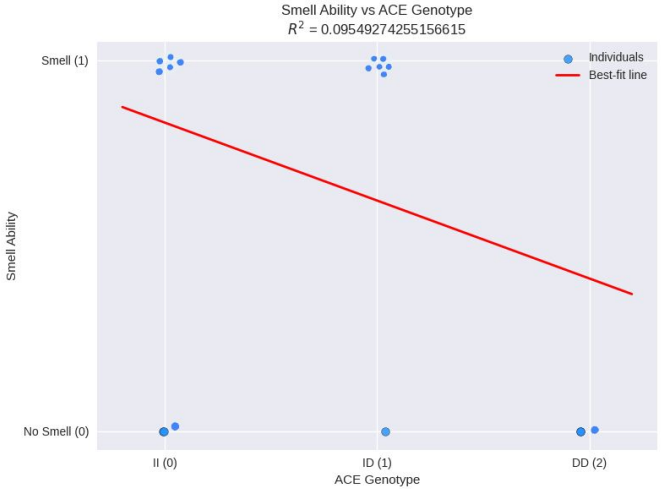


Genotype of Taste	Senses of Taste Affected	Genotype of No Taste	Sense of Taste Not Affected
—	1	—	3
II	4	II	2
II	13	II	15
II	14	II	16
ID	8	II	18
ID	9	ID	5
ID	10	ID	6
ID	11	ID	7
		DD	12
		DD	17

Participants Who Lost Their Sense of Smell

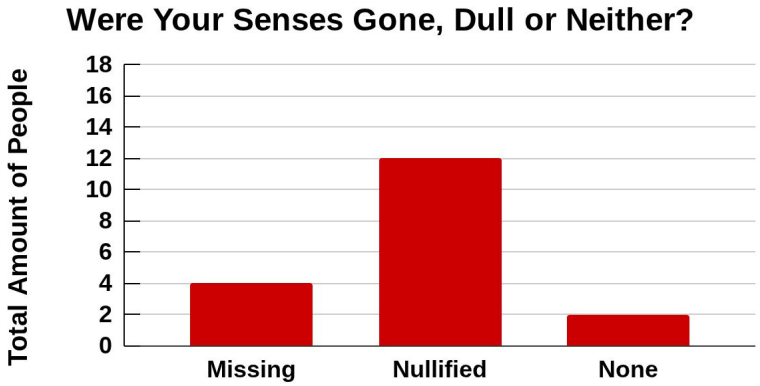


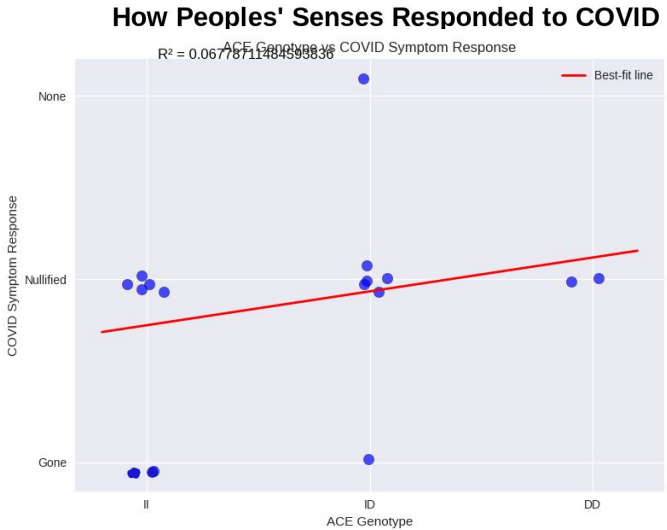
People Who Experienced Smell



Genotype of Smell	Sense of Smell Affected	Geno type of No Smell	Sense of Smell Not Affected
—	1	–	3
II	2	II	14
II	4	II	18
II	13	ID	5
II	15	DD	12
II	16	DD	17
ID	6		
ID	7		
ID	8		
ID	9		
ID	10		
ID	11		

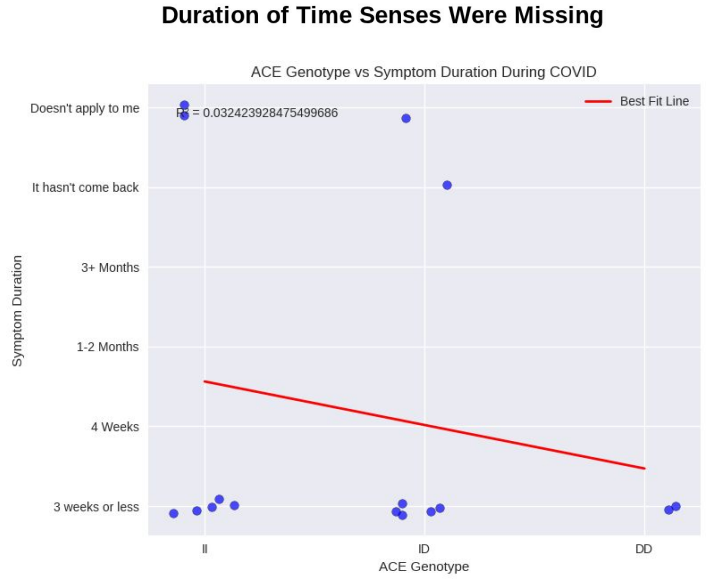
How Participants Senses Reacted to COVID





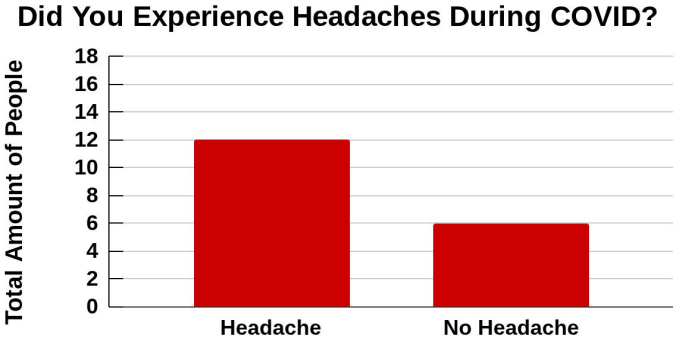
Genotype	Patient #	Senses Reaction
—	1	Gone
—	3	None
II	2	Gone
II	4	Nullified
II	13	Nullified
II	15	Nullified
II	14	Gone
II	16	Nullified
II	18	Nullified
ID	5	None
ID	6	Nullified
ID	7	Gone
ID	8	Nullified
ID	9	Nullified
ID	10	Nullified
ID	11	Nullified
DD	12	Nullified
DD	17	Nullified

Duration Participants Senses Were Gone For

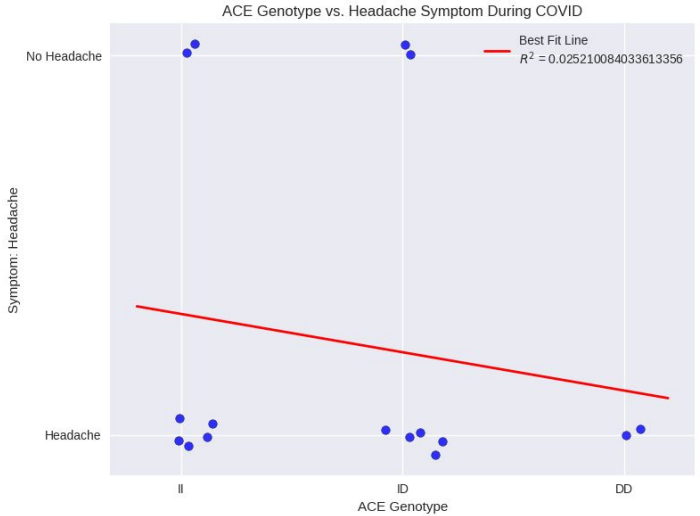


Genotype	Patient #	Duration Senses were Gone For
—	1	3 weeks or less
—	3	Doesn't apply
II	2	3 weeks or less
II	4	3 weeks or less
II	13	Doesn't apply
II	15	3 weeks or less
II	14	3 weeks or less
II	16	3 weeks or less
II	18	Doesn't apply
ID	5	Doesn't apply
ID	6	3 weeks or less
ID	7	3 weeks or less
ID	8	It hasn't come back
ID	9	3 weeks or less
ID	10	3 weeks or less
ID	11	3 weeks or less
DD	12	3 weeks or less
DD	17	3 weeks or less
		4 Weeks
		1-2 Months
		3+ Months

Participants Who Experienced Headaches

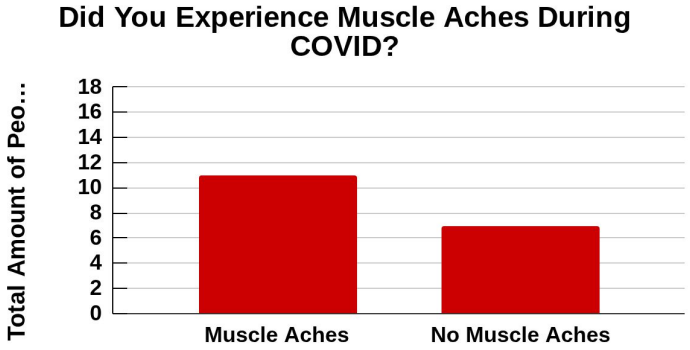


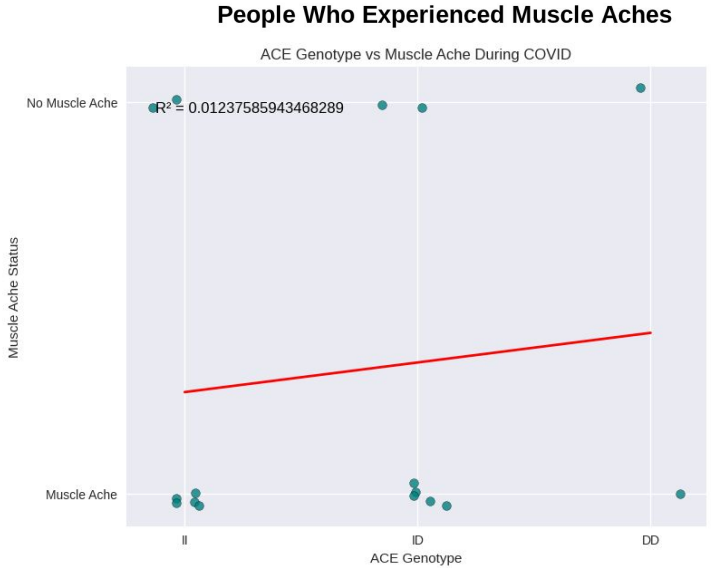
People Who Experienced Headaches



Genotype of Headache	Headache	Genotype of No Headache	No Headache
II	4	—	1
II	13	—	3
II	15	II	2
II	16	II	14
II	18	ID	10
ID	11	ID	8
ID	9		
ID	5		
ID	6		
ID	7		
DD	12		
DD	17		

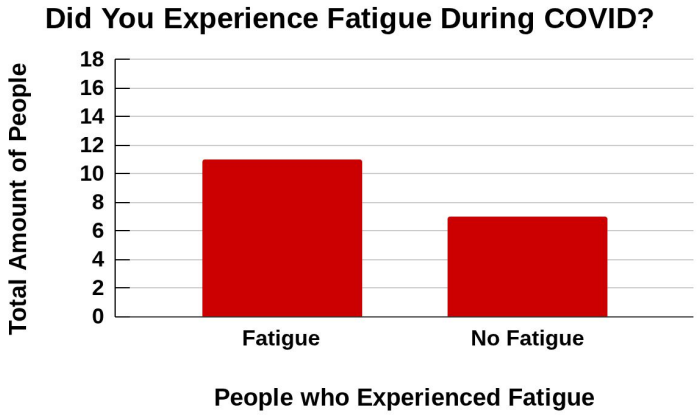
Participants Who Experienced Muscle Aches

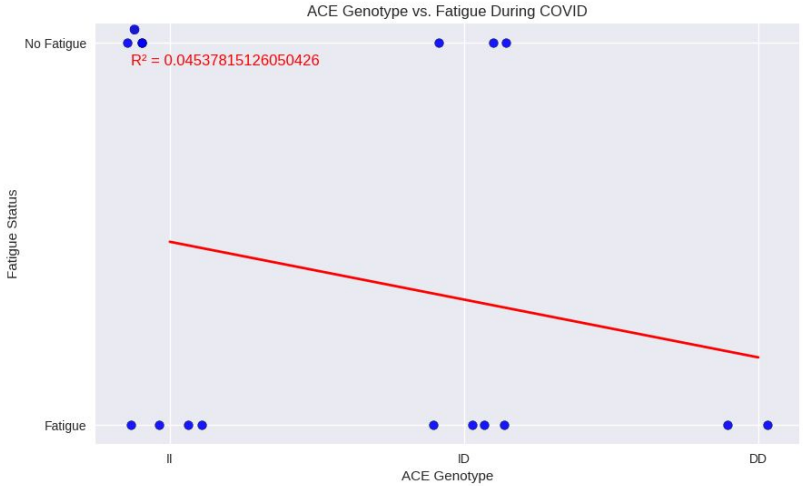




Genotype of Muscle Ache	Muscle Ache	Genotype of No Muscle Ache	No Muscle Ache
II	4	—	1
II	13	—	3
II	15	II	2
II	16	II	14
II	18	ID	11
ID	10	ID	8
ID	9	DD	17
ID	5		
ID	6		
ID	7		
DD	12		

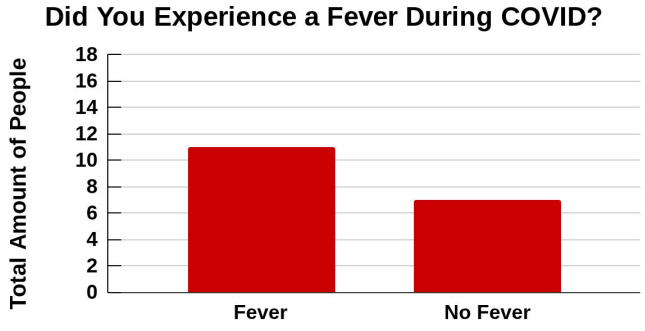
Participants Who Experienced Fatigue

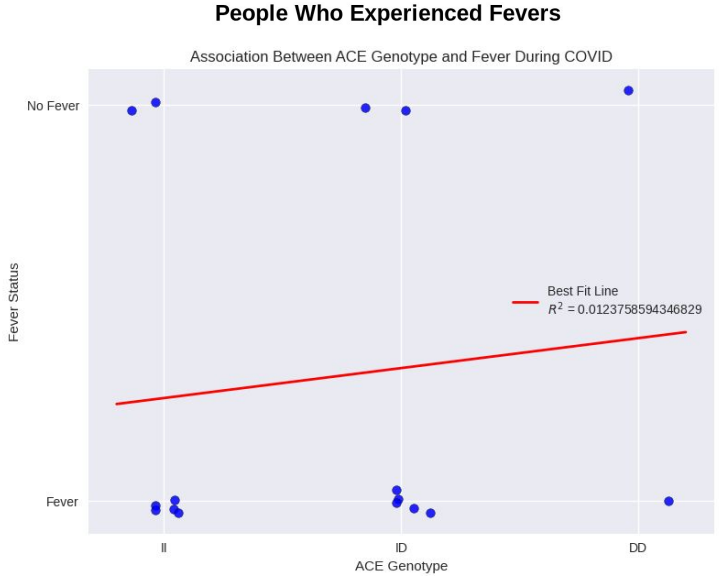




Genotype of Fatigue	Fatigue	Genotype of No Fatigue	No Fatigue
—	3	—	1
II	4	II	2
II	16	II	14
II	13	II	15
II	18	ID	10
ID	11	ID	6
ID	9	ID	8
ID	7		
ID	5		
DD	17		
DD	12		

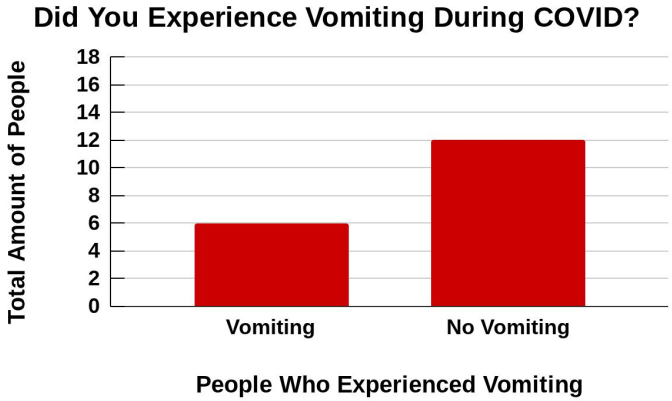
Participants Who Experienced A Fever

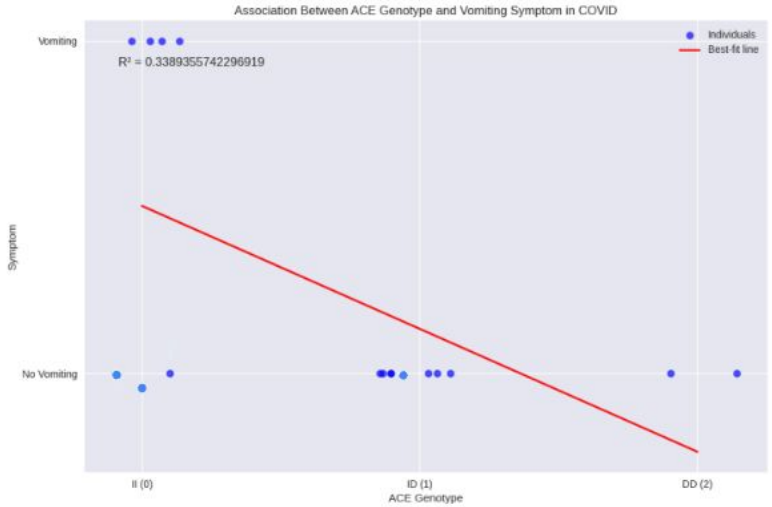




Genotype of Fever	Fever	Genotype of No Fever	No Fever
II	4	—	1
II	13	—	3
II	15	II	2
II	16	II	14
II	18	II	11
ID	10	ID	8
ID	9	DD	17
ID	5		
ID	6		
ID	7		
DD	12		

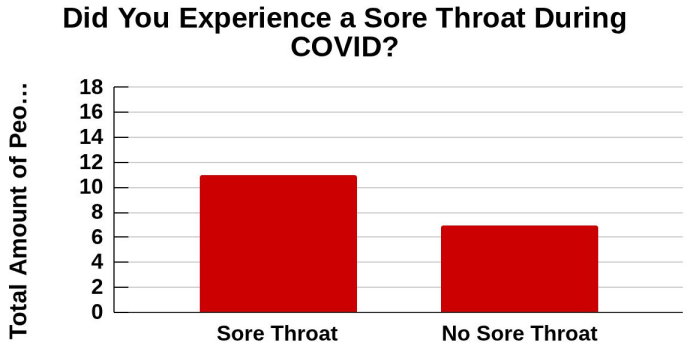
Participants Who Experienced Vomiting



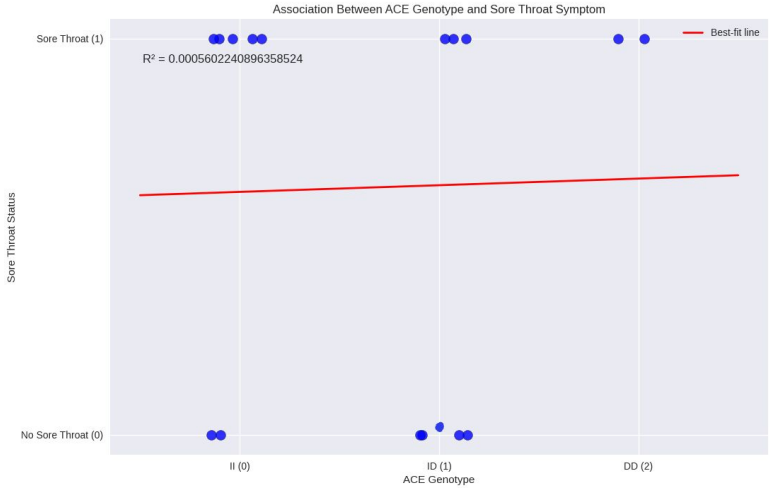


Genotype of Vomiting	Vomiting	Genotype of No Vomiting	No Vomiting
—	1	II	18
—	3	II	16
II	2	II	14
II	4	ID	8
II	13	ID	9
II	15	ID	10
		ID	11
		ID	5
		ID	7
		ID	6
		DD	17
		DD	12

Participants Who Experienced Sore Throat



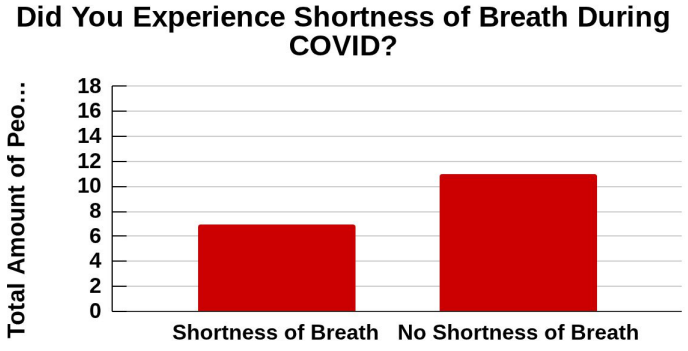
People Who Experienced a Sore Throat



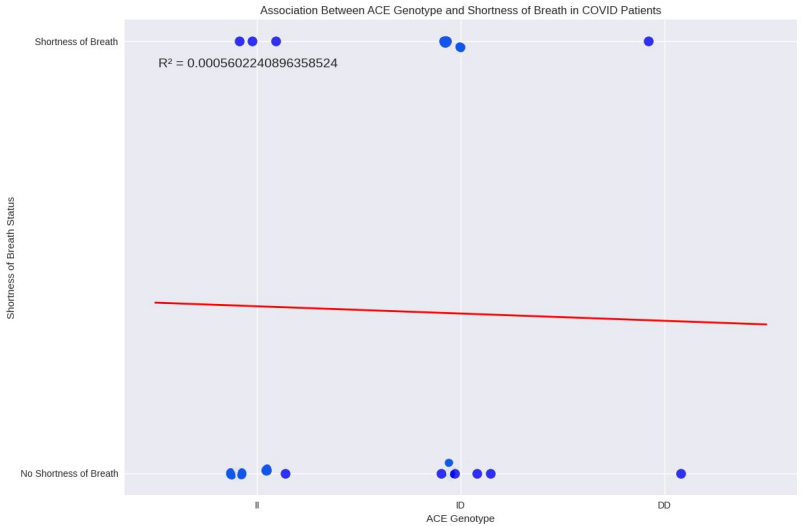
Genotype of Sore Throat	Sore Throat	Genotype of No Sore Throat	No Sore Throat
—	1	—	3
II	4	II	2
II	18	II	14
II	16	ID	9
II	15	ID	10
II	13	ID	11
ID	5	ID	8
ID	7		
ID	6		
DD	17		
DD	12		

Participants Who Experienced Shortness of Breath

~



People Who Experienced Shortness of Breath



Genotype of Shortness of Breath	Shortness of Breath	Genotype of No Shortness of Breath	No Shortness of Breath
—	1	—	3
II	4	II	2
II	15	II	13
II	18	II	14
ID	7	II	16
ID	9	ID	10
DD	12	ID	11
		ID	5
		ID	6
		ID	8
		DD	17

Patient #	Genotype
1	--
2	II
3	--
4	II
5	ID
6	ID
7	ID
8	ID
9	ID
10	ID
11	ID
12	DD
13	II
14	II
15	II
16	II
17	DD
18	II

Relationship between Participants and Genotypes

Percentage of the Patients Symptoms that are Explained By Their Genotype (Rounded to the nearest .01)

Statistical Analysis	R^2
COVID Infection Frequency	15.71%
COVID Duration	.3%
Vaccination Timing	19.67%
Symptom Response	6.78%
Sensory Symptoms	27.71%
Sensory Symptom: Taste	2.25
Sensory Symptom: Smell	9.55%
Sensory Symptom Duration	3.24%
Headache	2.52%
Muscle Ache	1.24%
Fever	1.24%
Fatigue	4.54%
Vomiting	33.89%
Nausea	2.52%
Sore Throat	.06%
Shortness of Breath	.06%

Results and Conclusion

The data that supported my hypothesis was Vomiting at a 33.89%, as there was 4 people who experienced vomiting and all had the II allele. Everyone who didn't experience vomiting were 3 people with the II allele, 7 people with the ID allele, and 2 people with the DD allele. Meaning this means that the II genotype may affect gastrointestinal disorders (GI)--which affect the digestive tract, and occurs when the digestive system isn't functioning properly. The upper GI is nausea and vomiting which is 2.52% correlation with nausea and 33.89% correlation with vomiting. Also sensory symptoms with 27.71%, which I broke down into two smaller sets of data which actually was 9.55% smell and 2.25% taste, which is smaller individually because the ACE gene probably interacts with other genes as well .Within a range of 10-20% with further information it would still support the hypothesis. Which is Covid infection frequency with 15.71% and Vaccination Timing with 19.67%. All other symptoms were under 10%, meaning they don't support my hypothesis.

Results and Conclusion

This could help with further research to see which ACE genotype influences gut dysbiosis the most (an imbalance in microbial community in the digestive tract) since COVID is already known to set an imbalance in the gut microbiome and also as it's known to be more of a respiratory disease. Overall this project provides how the ACE2 genotypes affect symptoms of COVID and gives further research into a new virus which could help people take more precaution when ill.

Bibliography

1) "COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection." *PubMed Central*, 3 January 2021, https://pmc.ncbi.nlm.nih.gov/articles/PMC7778857/. Accessed 5 December 2025.

2) Hu, Pan et al. "Human ACE2 Polymorphisms from Different Human Populations Modulate SARS-CoV-2 Infection." *Viruses* vol. 14,7 1451. 30 Jun. 2022, doi:10.3390/v14071451

3) Sriram, Krishna, et al. "What Is the ACE2 Receptor, How Is It Connected to Coronavirus and Why Might It Be Key to Treating COVID-19? The Experts Explain." *The Conversation*, 14 May 2020, https://doi.org/10.64628/AAI.r95ae53f4.

4) Strafella, Claudia, et al. "Analysis of ACE2 Genetic Variability among Populations Highlights a Possible Link with COVID-19-Related Neurological Complications." *Genes*, vol. 11, no. 7, July 2020, p. 741. *DOI.org (Crossref)*, https://doi.org/10.3390/genes11070741.

5) Oudit, Gavin Y., et al. "Angiotensin-Converting Enzyme 2—at the Heart of the COVID-19 Pandemic." *Cell*, vol. 186, no. 5, Mar. 2023, pp. 906–22. *ScienceDirect*, https://doi.org/10.1016/j.cell.2023.01.039.

6) *ACE Gene: MedlinePlus Genetics*. 1 May 2013, https://medlineplus.gov/genetics/gene/ace/.