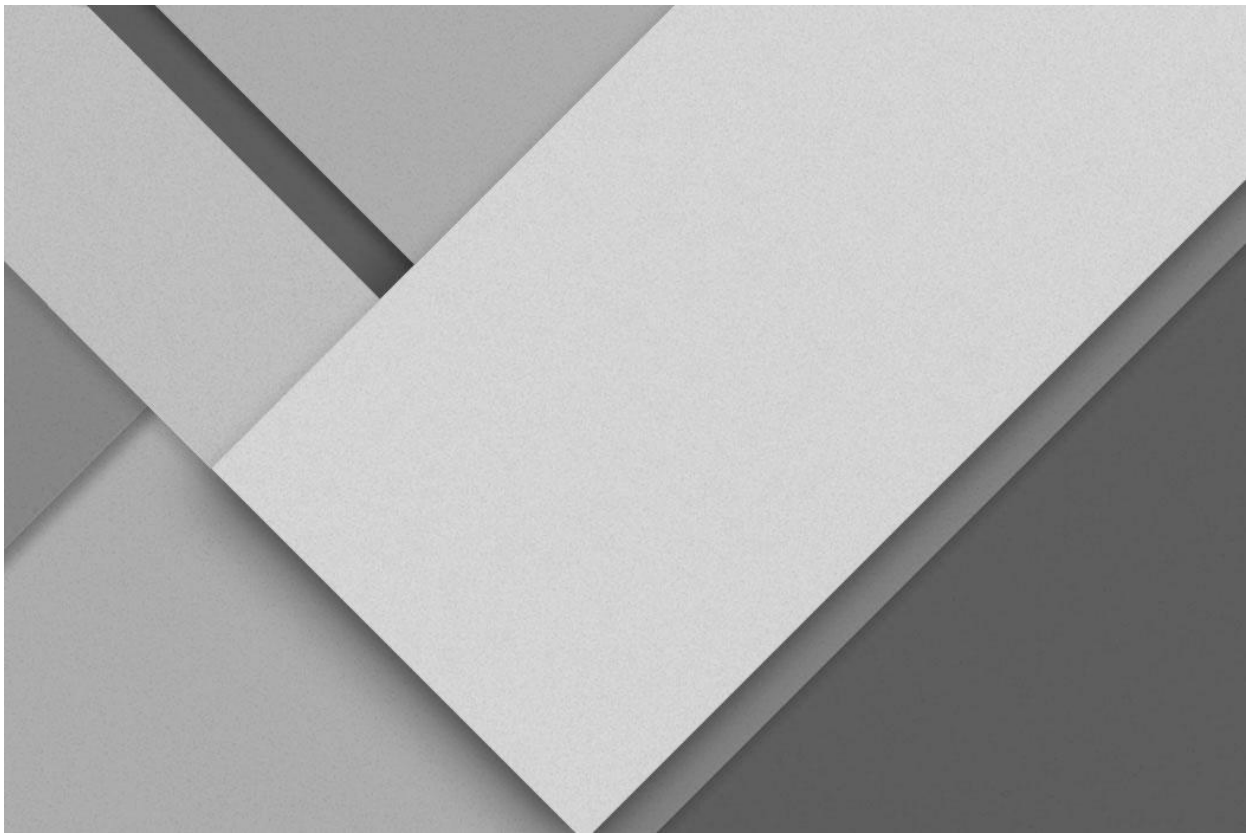


The significance of cerebrospinal fluid protein biomarkers in predicting cognitive decline in transient ischemic attack patients

Science Fair

—

Cole Lam

Dr. Philip A. Barber, Britney Denroche, Bhavana Gill

SEPTEMBER

SUN	MON	TUE	WED	THU	FRI	SAT
1	2	3 !! Send mentors email with September dates	4 ASP Class - Logbook Overview	5	6 ASP Class - Work Block	7
8	9	10 ASP Class - Meeting with Dr. Garcia; Read *White matter tract microstructure and cognitive performance after* TIA	11	12 ASP Class - Read *White matter tract microstructure and cognitive performance after TIA*	13	14
15	16 ASP Class - Project Proposal Overview	17	18 *ASP Class* - Read *A longitudinal MRI study of neurodegenerative and SVD [...]: the PREVENT study*	19	20 Meeting with Dr. Barber (12:00 PM - 1:00 PM) ASP Class - Meeting with Dr. Garcia	21
22	23 Print off APOE genotype articles	24 ASP Class - Read *Mixed brain pathologies account for most dementia cases in community -dwelling older persons*	25	26 ASP Class - Read *APOE and AD: Advances in Genetics, Pathophysiology, and Therapeutic Approaches.*	27	28
29	30 !! Logbook Due ! Send follow-up email for next meeting ASP Class - Read Literature	<u>Monthly Goals:</u> - Begin project proposal - Develop understanding of base knowledge in APOE genotyping				

OCTOBER

SUN	MON	TUE	WED	THU	FRI	SAT
		1	2 ASP Class - Meeting with Dr. Garcia; Research APOE and its association with AD	3	4 Meeting with Dr. Barber (10:30 AM) ASP Class - Research role of APOE; finish Introduction of project proposal	5
6	7 ! Send UCalgary email to Dr. Barber	8 ! Finish APOE genotype articles ASP Class - Draft Project Proposal (Background)	9	10 ASP Class - Draft Project Proposal (Expected Results, edit other sections)	11 !! Complete first draft of project proposal (and send to Dr. Barber)	12 !! Register for the IRISS
13	14	15 Meeting with Dr. Barber (10:30 AM) ASP Class - Meeting with Dr. Garcia	16	17 ASP Class - Edit Project Proposal (Methodology)	18	19
20 !!! Complete TCPS2	21 ASP Class - Edit Project Proposal (Overall)	22	23 Meeting with Dr. Barber (10:30 AM) ASP Class - Edit Project Proposal (All)	24	25 ASP Class - Meeting with Dr. Garcia	26 !!! Complete project proposal (and send to Dr. Barber)
27 !!! Complete CITI (not met)	28	29 ASP Class - Prepare Oral Presentation (Introduction, Goals)	30 Meeting with Dr. Barber (10:30 AM)	31 !! Logbook Due !!! Project Proposal Due Date !!! Complete CITI ASP Class - Finalize project proposal	<u>Monthly Goals:</u> - Finish project proposal - Complete ethics courses	

NOVEMBER

SUN	MON	TUE	WED	THU	FRI	SAT
					1	2
3	4 Send update email to Dr. Barber ASP Class - Prepare Oral Presentation (All)	5	6 ASP Class - Oral Presentations	7	8 !!! Oral Presentation Due ASP Class - Oral Presentations	9
10 !!! Complete blood work ethics courses	11	12	13 ASP Class - Oral Presentations	14	15 ASP Class - Read into PCR analysis for APOE genotyping	16
17	18 Send update email to Dr. Barber	19 ASP Class - Read into CSVD sum scores	20	21 ASP Class - Meeting with Dr. Garcia	22	23
24	25 ASP Class - Draft Introduction for final paper	26	27 ASP Class - Draft Introduction for final paper	28	29 ASP Class - Other School Work	30 !!! Submit Significant Risk 2B form for CYSF !! Logbook due

Monthly Goals:

- Oral Presentation
- Begin drafting Introduction and Methodology for final paper

DECEMBER

SUN	MON	TUE	WED	THU	FRI	SAT
1	2	3 ASP Class - Lost to Presidents' Breakfast	4 Follow-up to Dr. Barber about data analysis and moving forward	5 ASP Class - Finalize CYSF Portal (as far as possible)	6	7
8	9 ASP Class - Meeting with Dr. Garcia; Work on Introduction for Final Paper	10	11 ASP Class - Work on Introduction for Final Paper	12	13 ASP Class - Work on Methodology for Final Paper Send an update email to Dr. Barber	14
15	16	17 ASP Class - Meeting with Dr. Garcia; Work on Methodology for Final Paper	18	19 ASP Class - Flex Remind Dr. Barber winter break and midterm restrictions	20	21
22	23	24	25	26	27	28
29	30	<u>Monthly Goals:</u> - Complete a sizeable portion of my final research paper (Introduction, Methodology)				

JANUARY

SUN	MON	TUE	WED	THU	FRI	SAT
			1	2	3	4
5	6 ASP Class - Midterm Review	7 ~~!!! Data collection observation (9:00 AM - 1:00 PM)~~	8 ASP Class - Midterm Review	9	10	11
12	13	14	15	16	17	18
19	20	21	22 ASP Class - Research Paper Introduction (Summary Statistics)	23	24 Meeting with Britney and Bhavana (1:00 PM) ASP Class - Research Paper Introduction (TIA, dementia)	25
26	27	28 ASP Class - Research Paper Introduction (TIA, dementia)	29	30 !! Research Paper Introduction Due (Postponed) Meeting with Britney and Bhavana (10:30 AM) ASP Class - Research Paper Introduction (CSF)	31 !! Logbook due	

Monthly Goals:

- Finish research paper introduction
- ~~Observe data collection at the University~~
- Begin data analysis

FEBRUARY

SUN	MON	TUE	WED	THU	FRI	SAT
						1
2	3 ASP Class - Research Paper (Introduction and Methodology)	4	5 ASP Class - Statistical Analysis (Introduction Final Edits)	6	7 !! Research Paper Introduction Due (Tentative) Meeting with Bhavana (10:20 AM) ASP Class - Statistical Meeting	8 ASP Work - Descriptive Tests and T-Tests for CSF and demographic data
9	10	11 ASP Class - Statistical Analysis (Linear regression models)	12 !! Meeting with Bhavana at 11:35 AM	13 ASP Class - Statistical Analysis (Linear regression analysis)	14	15
16 ASP Work - Methods Paper Final Edits	17	18	19 !! Research Paper Methodology Due ASP Class - Meeting with Dr. Garcia; Science Fair Prep (Poster board)	20	21 ASP Class - Science Fair Prep (Write Oral Presentation)	22 ASP Work - Write Oral Presentation
23 ASP Work - Finalized Science Fair Poster	24 Science Fair Mock Presentation for Dr. Garcia	25 !! Meeting with Bhavana at 8:30 AM ASP Class - Science Fair Prep (Finalize Oral Presentation)	26	27 !!! Science Fair Presentation !! Finalized Science Fair Poster ASP Class - Science Fair Presentations	28	

Monthly Goals:

- Finish research paper introduction and methodology sections
- Complete data collection
- Prepare for science fair

MARCH

SUN	MON	TUE	WED	THU	FRI	SAT
						1
2	3 ASP Class - Finalize Science Fair Oral Presentation (Shorten to 10-12 minutes)	4	5 ASP Class - Finalize poster (and prepare for printing); communicate with mentors	6	7 ASP Class - Begin writing Results Paper (add figures?)	8
9	10	11 !!! Webber Academy Internal Science Fair ~~ASP Class~~	12	13 ASP Class - Results Paper (Text and Figure Descriptions)/CYSF Portal Information	14	15
16	17 ASP Class - Results Paper Final Edits (Run paper by Dr. Garcia?)	18	19 ASP Class - Results Paper Final Edits (Run paper by Dr. Garcia?)	20	21 ~~!!! Research Paper Results Due~~ ASP Class - CYSF Portal Information Finalization/Results Paper Edits	22
23	24	25	26	27	28 !!! CYSF Portal Information Due	29
30	31					

Monthly Goals:

- Prepare for science fair
- Compose results section for research paper

Daily Notes

July 22, 2024

Tasks To-do	Review	Notes
☐ Arrange a date to meet Dr. Barber in August (New)	Dr. Garcia and I met with Dr. Barber's assistants, Bhavana Gill and Britney Denroche. Discussion included what the Applied Science Project is, and what my project should look like. Specifically, that the timeframe of the project shouldn't be too long, and that my project doesn't need to be incredibly complex.	1. Dr. Barber was on vacation, so he could not meet.

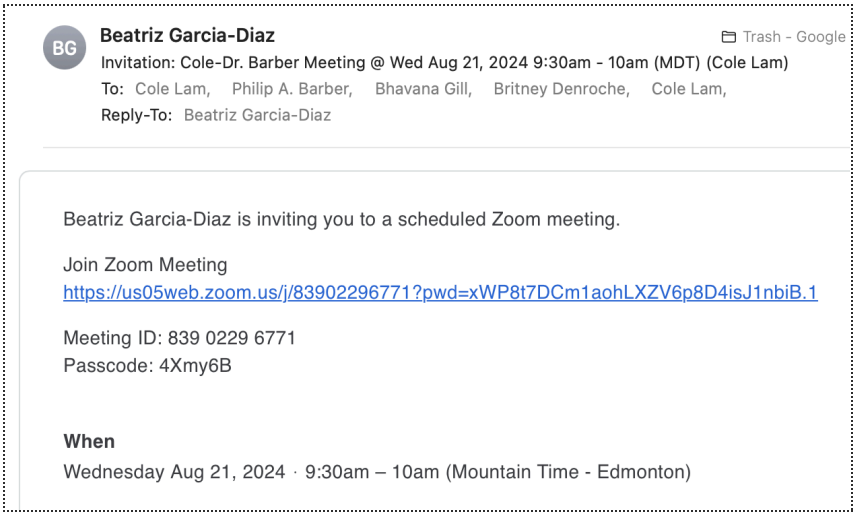
Tasks Completed
None

August 15, 2024

Tasks To-do	Tasks Completed	Notes
☐ Create logbook (New)	☑ Arrange a date to meet Dr. Barber in August	None

Review

Through email, Dr. Garcia, Bhavana, Britney, Dr. Barber, and I decided on a date and time to meet for a second time to further discuss my project (Aug. 21, 9:30 AM).



BG **Beatriz Garcia-Diaz** Trash - Google

Invitation: Cole-Dr. Barber Meeting @ Wed Aug 21, 2024 9:30am - 10am (MDT) (Cole Lam)

To: Cole Lam, Philip A. Barber, Bhavana Gill, Britney Denroche, Cole Lam,

Reply-To: Beatriz Garcia-Diaz

Beatriz Garcia-Diaz is inviting you to a scheduled Zoom meeting.

Join Zoom Meeting
https://us05web.zoom.us/j/83902296771?pwd=xWP8t7DCm1aohLXZV6p8D4isJ1nbiB.1

Meeting ID: 839 0229 6771
Passcode: 4Xmy6B

When
Wednesday Aug 21, 2024 · 9:30am – 10am (Mountain Time - Edmonton)

August 21, 2024

Tasks To-do

- [ ] Share timetable/ free days (New)
- [ ] Create logbook

Tasks Completed

None

Review

Dr. Garcia and I met Dr. Barber and his assistants to clarify details regarding how my project should be structured, and what I should begin doing in the coming weeks. Specifically, Dr. Garcia mentioned that my project proposal needs to be in by mid to end October, and for now, we should work on coming up with a project that I can work on/contribute to. For now, they would send me some literature to begin reading to get an idea of the background information necessary for fulfilling my role, and that they would discuss projects I could work on for the next/future meetings.

Notes

1. Bhavana and Britney would send me literature to begin reading sometime in the coming weeks.
2. Make sure to include all meetings over the summer in the logbook.

August 30, 2024

Tasks To-do

- [ ] Share timetable/ free days

Tasks Completed

- [x] Create logbook

Review

This class, Dr. Garcia covered how our project will go this year. Specifically, it included what our projects look like (ie. project proposal, logbook, presentations, science fair, mock paper) and over how we should plan to communicate with our mentors, how frequently, and how most importantly, this course is self-driven and that we are responsible for our conduct throughout this course. We also went over the course outline (Outline ASP 2024-2025.pdf) and our mark breakdown (Categories Weighting ASP2024-2025.pdf). Finally, we covered the tips that Dr. Garcia could tell us from past years' experiences, such as to make sure that we continuously stay in contact with mentors, that we ensure that we are organized (both in terms of our work and logbook), and that we remain productive during all of our work blocks (and don't go to the cafeteria "black hole").

Notes

1. First class of the school year.
2. Schedules were released and extracurriculars were starting, so we should update our mentors about availability for the coming months.

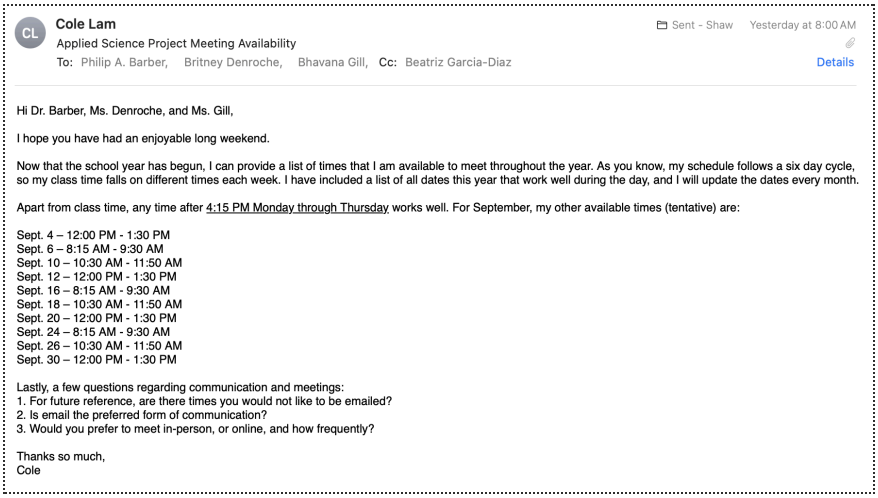
Daily Notes

September 3, 2024

Tasks To-do	Tasks Completed	Notes
☐ Decide on days to meet with mentors for September (New)	☑ Share timetable and available days	1. Follow up on emails 3-5 business days after sending, if necessary.

Review

After the Labour Day long weekend, I sent out an email to Dr. Barber, Britney, and Bhavana that included a document listing all of my classes throughout the year which I could use to meet either virtually or in-person with them (Cole Lam - Applied Science Project Meeting Availability). I also clarified the other times I am free to meet, and included a few logistical questions, such as how we should communicate in the future and how often.



CL **Cole Lam** — Sent - Shaw — Yesterday at 8:00 AM

Applied Science Project Meeting Availability

To: Philip A. Barber, Britney Denroche, Bhavana Gill, Cc: Beatriz Garcia-Diaz — Details

Hi Dr. Barber, Ms. Denroche, and Ms. Gill,

I hope you have had an enjoyable long weekend.

Now that the school year has begun, I can provide a list of times that I am available to meet throughout the year. As you know, my schedule follows a six day cycle, so my class time falls on different times each week. I have included a list of all dates this year that work well during the day, and I will update the dates every month.

Apart from class time, any time after 4:15 PM Monday through Thursday works well. For September, my other available times (tentative) are:

Sept. 4 – 12:00 PM - 1:30 PM
Sept. 6 – 8:15 AM - 9:30 AM
Sept. 10 – 10:30 AM - 11:50 AM
Sept. 12 – 12:00 PM - 1:30 PM
Sept. 16 – 8:15 AM - 9:30 AM
Sept. 18 – 10:30 AM - 11:50 AM
Sept. 20 – 12:00 PM - 1:30 PM
Sept. 24 – 8:15 AM - 9:30 AM
Sept. 26 – 10:30 AM - 11:50 AM
Sept. 30 – 12:00 PM - 1:30 PM

Lastly, a few questions regarding communication and meetings:
1. For future reference, are there times you would not like to be emailed?
2. Is email the preferred form of communication?
3. Would you prefer to meet in-person, or online, and how frequently?

Thanks so much,
Cole

September 4, 2024

Tasks To-do

- [ ] Decide on days to meet with mentors for September

Tasks Completed

None

Review

This class, we covered how our logbook should be organized and its importance. Dr. Garcia provided us with a document outlining her recommended structure for the research logbook, along with its requirements (Guidelines for Logbook.pdf). Other information included the platforms we could work on our logbooks from (ie. Google Docs, Word, Notion, etc.) She also introduced our first major writing assignment, our research proposal, which should be completed sometime in mid-October.

Notes

1. Follow up on emails 3-5 business days after sending, if necessary.

September 6, 2024

Tasks To-do

- [ ] Decide on days to meet with mentors for September
- [ ] Read the literature sent by Dr. Barber (New)

Tasks Completed

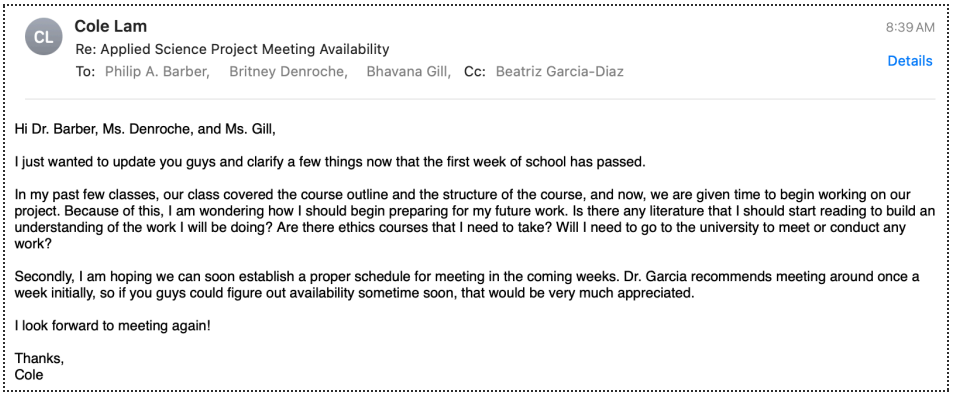
None

Notes

None

Review

By this class, I was still waiting to hear from my mentors regarding the next steps for the project, so I composed a follow-up email asking about what to do next. Dr. Barber responded by telling me that he will update me some time next week when he has more time. Apart from this, I spent the block organizing my logbook and all of its sections.



CL **Cole Lam** 8:39 AM

Re: Applied Science Project Meeting Availability

To: Philip A. Barber, Britney Denroche, Bhavana Gill, Cc: Beatriz Garcia-Diaz Details

Hi Dr. Barber, Ms. Denroche, and Ms. Gill,

I just wanted to update you guys and clarify a few things now that the first week of school has passed.

In my past few classes, our class covered the course outline and the structure of the course, and now, we are given time to begin working on our project. Because of this, I am wondering how I should begin preparing for my future work. Is there any literature that I should start reading to build an understanding of the work I will be doing? Are there ethics courses that I need to take? Will I need to go to the university to meet or conduct any work?

Secondly, I am hoping we can soon establish a proper schedule for meeting in the coming weeks. Dr. Garcia recommends meeting around once a week initially, so if you guys could figure out availability sometime soon, that would be very much appreciated.

I look forward to meeting again!

Thanks,
Cole

PB **Philip A. Barber**

Re: Applied Science Project Meeting Availability

To: Cole Lam, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz

Hi Cole
I am just finishing clinical service. I will get back to you early next week.
Best wishes
Philip Barber

Later this evening, Dr. Barber sent me an email listing some reading material that I should start reading. There were 23 articles, about half of which he published, and the others outlining principal ideas that are important for the types of projects he is working on.

PB **Philip A. Barber** September 6, 2024 at 5:10 PM

Re: Applied Science Project Meeting Availability Details

To: Cole Lam, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz

Hi Cole
I am attaching some reading material.
PB

1. Tariq S, **Barber PA**. Dementia risk and prevention by targeting modifiable vascular risk factors. J Neurochem 2018;144:565-581.
2. Corrada MM, Brookmeyer R, Paganini-Hill A, Berlau D, Kawas CH. Dementia incidence continues to increase with age in the oldest old: the 90+ study. Ann Neurol 2010;67:114-121.
3. Blennow K, Hampel H, Zetterberg H. Biomarkers in amyloid-Î² immunotherapy trials in Alzheimer's disease. Neuropsychopharmacology 2014;39:189-201.

7. Ganesh A, **Barber PA**. The Cognitive Sequelae of Transient Ischemic Attacks-Recent Insights and Future Directions. J Clin Med 2022;11.
8. Daniel A. Nation MDS, Axel Montagne, Abhay P. Sagare, Lina M. D'Orazio, Maricarmen Pachicano, Farshid Sepehrband, Amy R. Nelson, David P. Buennagel, Michael G. Harrington, Tammie L.S. Benzinger, Anne M. Fagan, John M. Ringman, Lon S. Schneider, John C. Morris Helena C. Chui, Meng Law, Arthur W. Toga, and Berislav V. Zlokovic. Blood-brain barrier breakdown is an early biomarker of human cognitive dysfunction. Nature medicine 2019;25(2): 270–276. doi:10.1038/s41591-018-0297-y.
13. Ryan NS, Biessels G-J, Kim L, Nicholas JM, **Barber PA**, Walsh P, Gami P, Morris HR, Bastos-Leite AnJ, Schott JM, Beck J, Mead S, Chavez-Gutierrez L, de Strooper B, Rossor MN, Revesz T, Lashley T, Fox NC. Genetic determinants of white matter hyperintensities and amyloid angiopathy in familial Alzheimer's disease. Neurobiology of aging 2015;36:3140-3151.
14. Shirzadi Z, Schultz SA, Yau W-YW, Joseph-Mathurin N, Fitzpatrick CD, Levin R, Kantarci K, Preboske GM, Jack CR, Jr, Farlow MR, Hassenstab J, Jucker M, Morris JC, Xiong C, Karch CM, Levey AI, Gordon BA, Schofield PR, Salloway SP, Perrin RJ, McDade E, Levin J, Cruchaga C, Allegri RF, Fox NC, Goate A, Day GS, Koeppe R, Chui HC, Berman S, Mori H, Sanchez-Valle R, Lee J-H, Rosa-Neto P, Ruthirakuhan M, Wu C-Y, Swardfager W, Benzinger TLS, Sohrabi HR, Martins RN, Bateman RJ, Johnson KA, Sperling RA, Greenberg SM, Schultz AP, Chhatwal JP, Network DIA, Initiative tAsDN. Etiology of White Matter Hyperintensities in Autosomal Dominant and Sporadic Alzheimer Disease. JAMA neurology 2023;80:1353-1363.
18. **Barber P**, Nestor SM, Wang M, Wu P, Ursenbach J, Munir A, Gupta R, Tariq SS, Smith E, Frayne R, Black SE, Sajobi T, Coutts S. Hippocampal atrophy and cognitive function in transient ischemic attack and minor stroke patients over three years. Cerebral Circulation - Cognition and Behavior 2021;2:100019.

19. Reaume N, Reid M, Tadros GS, Chacinski D, Denroche B, Aftab A, Wu P, Gupta Sah R, Wang M, **Smith EE, Frayne R, Coutts SB**, Sajobi T, Longman S, Ganesh A, **Barber PA**. The relationship of small vessel disease burden on cerebral and regional brain atrophy rates and cognitive performance over one year of follow-up after transient ischemic attack. Frontiers in Neurology 2023;14:1277765.
21. Tariq S, Tsang A, Wang M, Reaume N, Carlson H, Sajobi TT, Longman RS, **Smith EE, Frayne R**, d'Esterre CD, Coutts SB, **Barber PA**. White matter tract microstructure and cognitive performance after transient ischemic attack. PloS one 2020;15:e0239116.
28. Kalaria RN. Neuropathological diagnosis of vascular cognitive impairment and vascular dementia with implications for Alzheimer's disease. Acta neuropathologica 2016;131:659-685.
29. Pathological correlates of late-onset dementia in a multicentre, community-based population in England and Wales. Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS). Lancet 2001;357:169-175.
31. Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in community-dwelling older persons. Neurology 2007;69:2197-2204.
32. Schneider JA, Boyle PA, Arvanitakis Z, Bienias JL, Bennett DA. Subcortical infarcts, Alzheimer's disease pathology, and memory function in older persons. Ann Neurol 2007;62:59-66.
33. Sonnen JA, Larson EB, Crane PK, Haneuse S, Li G, Schellenberg GD, Craft S, Leverenz JB, Montine TJ. Pathological correlates of dementia in a longitudinal, population-based sample of aging. Ann Neurol 2007;62:406-413.
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36. van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, Kanekiyo M, Li D, Reyderman L, Cohen S, Froelich L, Katayama S, Sabbagh M, Vellas B, Watson D, Dhadda S, Irizarry M, Kramer LD, Iwatsubo T. Lecanemab in Early Alzheimer's Disease. N Engl J Med 2023;388:9-21.
37. Mintun MA, Lo AC, Duggan Evans C, Wessels AM, Ardayfio PA, Andersen SW, Shcherbinin S, Sparks J, Sims JR, Brys M, Apostolova LG, Salloway SP, Skovronsky DM. Donanemab in Early Alzheimer's Disease. N Engl J Med 2021;384:1691-1704.
38. Cummings J, Aisen P, Apostolova LG, Atri A, Salloway S, Weiner M. Aducanumab: Appropriate Use Recommendations. J Prev Alzheimers Dis 2021;8:398-410.
39. Hansson O. Biomarkers for neurodegenerative diseases. Nature medicine 2021;27:954-963.
40. Palmqvist S, Janelidze S, Quiroz YT, Zetterberg H, Lopera F, Stomrud E, Su Y, Chen Y, Serrano GE, Leuzy A, Mattsson-Carlgren N, Strandberg O, Smith R, Villegas A, Sepulveda-Falla D, Chai X, Proctor NK, Beach TG, Blennow K, Dage JL, Reiman EM, Hansson O. Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders. Jama 2020;324:772-781.
45. Keshavan A, Pannee J, Karikari TK, Rodriguez JL, Ashton NJ, Nicholas JM, Cash DM, Coath W, Lane CA, Parker TD, Lu K, Buchanan SM, Keuss SE, James SN, Murray-Smith H, Wong A, Barnes A, Dickson JC, Heslegrave A, Portelius E, Richards M, Fox NC, Zetterberg H, Blennow K, Schott JM. Population-based blood screening for preclinical Alzheimer's disease in a British birth cohort at age 70. Brain 2021;144:434-449.
57. Black S, Gao F, Bilbao J. Understanding white matter disease: imaging-pathological correlations in vascular cognitive impairment. Stroke 2009;40:S48-52.
59. A Classification and Outline of Cerebrovascular Diseases II.[Article]. Stroke 6(5):564-616, September/October 1975.

67. Tariq S, d'Esterre CD, Sajobi TT, **Smith EE, Longman RS, Frayne R, Coutts SB, Forkert ND, Barber PA**. A longitudinal magnetic resonance imaging study of neurodegenerative and small vessel disease, and clinical cognitive trajectories in non demented patients with transient ischemic attack: the PREVENT study. BMC geriatrics 2018;18:163.
91. Duering M, Biessels GJ, Brodtmann A, Chen C, Cordonnier C, de Leeuw F-E, Debette Sp, Frayne R, Jouvent E, Rost NS, ter Telgte A, Al-Shahi Salman R, Backes WH, Bae H-J, Brown R, Chabriat H, De Luca A, deCarli C, Dewenter A, Doubal FN, Ewers M, Field TS, Ganesh A, Greenberg S, Helmer KG, Hilal S, Jochems ACC, Jokinen H, Kuijf H, Lam BYK, Lebenberg J, MacIntosh BJ, Maillard P, Mok VCT, Pantoni L, Rudilosso S, Satizabal CL, Schirmer MD, Schmidt R, Smith C, Staals J, Thrippleton MJ, van Veluw SJ, Vemuri P, Wang Y, Werring D, Zedde M, Akinyemi RO, Del Brutto OH, Markus HS, Zhu Y-C, Smith EE, Dichgans M, Wardlaw JM. Neuroimaging standards for research into small vessel disease—advances since 2013. The Lancet Neurology 2023;22:602-618.
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106. **Smith EE**, Nandigam KR, Chen YW, Jeng J, Salat D, Halpin A, Frosch M, Wendell L, Fazen L, Rosand J, Viswanathan A, Greenberg SM. MRI markers of small vessel disease in lobar and deep hemispheric intracerebral hemorrhage. Stroke 2010;41:1933-1938.

September 8, 2024

Tasks To-do

- [ ] Decide on days to meet with mentors for September
- [ ] Read the literature sent by Dr. Barber
- [ ] Get the PDF documents for the articles (New)

Tasks Completed

None

Review

Today, I sent an email to one of my relatives to see if he could get me the PDF documents for the literature that Dr. Barber sent me.

Notes

None

September 9, 2024

Tasks To-do

- [ ] Decide on days to meet with mentors for September
- [ ] Read the literature sent by Dr. Barber
- [ ] Print of the PDF documents for annotations (New)

Tasks Completed

- [x] Get the PDF documents for the articles

Notes

1. Follow up on meeting times if no response by Thursday

Review

This morning, my relative sent me the articles to begin reading. I loaded the documents onto a USB stick so I could go out to print the documents.

September 10, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read the literature sent by Dr. Barber	☑ Print of the PDF documents for annotations ☑ Decide on days to meet with mentors for September	1. Read ~1 article/2 days

Review

During the ASP class, I had my meeting with Dr. Garcia about the course of action moving forward. Because another date to talk with Dr. Barber had not yet been established, we discussed what we should try and establish for the next meeting. This would include determining the project that I am doing (generally), specifically to determine what I can include in my project proposal, and what my goals, both short-term and long-term for the project may be. We also discussed the best way for me to read the literature, and that I can annotate the articles using Paperpile online, and export the annotations and PDFs; however, we decided that I would annotate printed versions of the documents and submit it in addition to my logbook as part of my background research.
Dr. Barber also emailed asking for available dates during the school day, so I sent him a document including all available times throughout the school year. The date that we decided on was September 20, from 12:00 PM - 1:00 PM.

PB **Philip A. Barber** 10:53 AM
Re: Applied Science Project Meeting Availability
To: Cole Lam, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz Details

Hi Cole,

We should arrange a regular time in the week to meet. Please provide some dates and times that would work with your school schedule.

PB

CL **Cole Lam** 10:58 AM
Re: Applied Science Project Meeting Availability
To: Philip A. Barber, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz Details

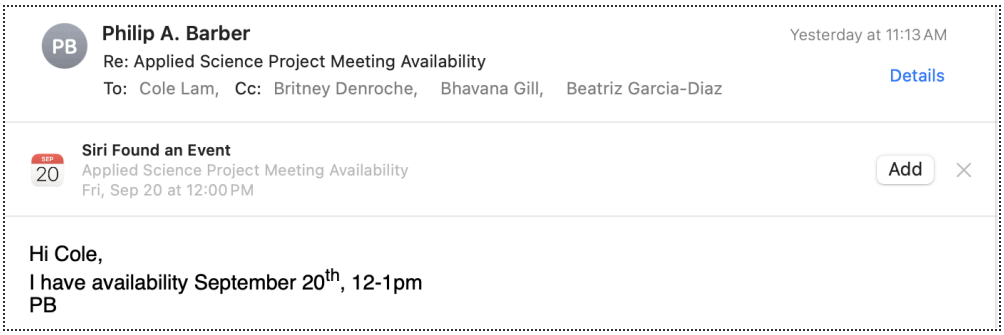
Good morning, Dr. Barber,

My available dates for September are:
Sept. 12 – 12:00 PM - 1:30 PM
Sept. 16 – 8:15 AM - 9:30 AM
Sept. 18 – 10:30 AM - 11:50 AM
Sept. 20 – 12:00 PM - 1:30 PM
Sept. 24 – 8:15 AM - 9:30 AM
Sept. 26 – 10:30 AM - 11:50 AM
Sept. 30 – 12:00 PM - 1:30 PM

Additionally, any time after 4:30 Monday through Thursday works for me, if you prefer later in the evening.

The document attached at the bottom of the email includes all dates and times throughout the school year, including those after September.

Best regards,
Cole



Philip A. Barber Yesterday at 11:13 AM
Re: Applied Science Project Meeting Availability
To: Cole Lam, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz Details

Siri Found an Event
Applied Science Project Meeting Availability
Fri, Sep 20 at 12:00 PM Add

Hi Cole,
I have availability September 20th, 12-1pm
PB

Lastly, I began reading and annotating one of the articles published by Dr. Barber, *White matter tract microstructure and cognitive performance after transient ischemic attack* (White matter tract microstructure and cognitive performance after transient ischemic attack).

September 11, 2024

Tasks To-do	Review	Notes
☐ Read the literature sent by Dr. Barber	This evening, after updating my logbook with dates and tasks, I continued annotating *White matter tract microstructure and cognitive performance after transient ischemic attack*. I also updated my Background Research section of my logbook, with comprehensive information from the article with more casual diction, as well as a 7 point summary of the entire article.	1. Read ~1 article/2 days

Tasks Completed
None

September 12, 2024

Tasks To-do	Review	Notes
☐ Read the literature sent by Dr. Barber	This day (both class and evening), I continued updating my logbook's background information while finishing *White matter tract microstructure and cognitive performance after transient ischemic attack* and reading *A Classification and Outline of Cerebrovascular Diseases II* (A Classification and Outline of Cerebrovascular Diseases II). I chose this article to help me develop a base level understanding of cerebrovascular diseases before reading articles which address more specific areas.	1. Read ~1 article/2 days

Tasks Completed
None

September 15, 2024

Tasks To-do	Review	Notes
☐ Read the literature sent by Dr. Barber	I continued reading *A Classification and Outline of Cerebrovascular Diseases II* . The progress was slow, because the literature included lots of vocabulary.	1. Read ~1 article/2 days

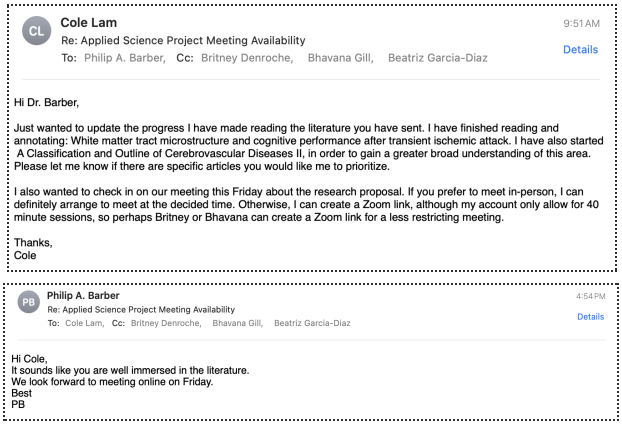
Tasks Completed
None

September 16, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read the literature sent by Dr. Barber	None	1. Read ~1 article/2 days

Review

In class, we focused on two things: how to use Paperpile for annotating and citing literature, and what our project proposal should include. Regarding the usage of Paperpile, Dr. Garcia clarified how to implement Paperpile into our logbooks, and what types of citations we want (AMA for medicine, APA for general science). Then, in talking about the research proposal, we covered the structure, including the title, which should be specific, the introduction, which is to include background information with statistics, along with controversies within the field, leading to the research question, the goals, and then the methods of the experiment. The introduction should be a target discussion for the first meeting, and the second meeting should start discussing the methods.
I also sent an email to Dr. Barber clarifying the logistics of the meeting on September 20.



Cole Lam 9:51 AM
Re: Applied Science Project Meeting Availability
To: Philip A. Barber, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz Details

Hi Dr. Barber,

Just wanted to update the progress I have made reading the literature you have sent. I have finished reading and annotating: White matter tract microstructure and cognitive performance after transient ischemic attack. I have also started A Classification and Outline of Cerebrovascular Diseases II, in order to gain a greater broad understanding of this area. Please let me know if there are specific articles you would like me to prioritize.

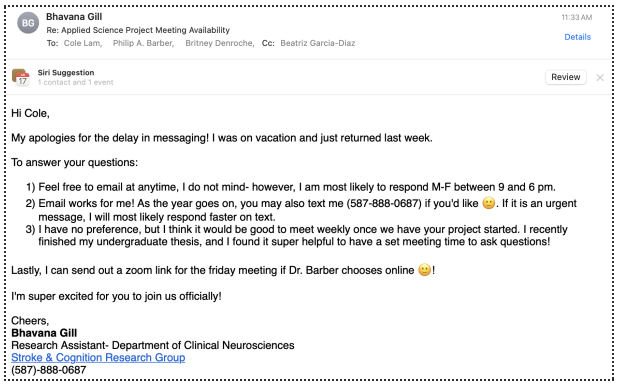
I also wanted to check in on our meeting this Friday about the research proposal. If you prefer to meet in-person, I can definitely arrange to meet at the decided time. Otherwise, I can create a Zoom link, although my account only allow for 40 minute sessions, so perhaps Britney or Bhavana can create a Zoom link for a less restricting meeting.

Thanks,
Cole

Philip A. Barber 4:54 PM
Re: Applied Science Project Meeting Availability
To: Cole Lam, Cc: Britney Denroche, Bhavana Gill, Beatriz Garcia-Diaz Details

Hi Cole,
It sounds like you are well immersed in the literature.
We look forward to meeting online on Friday.
Best
PB

I also got an email from Bhavana answering some of my questions from September 3rd.



Bhavana Gill 11:33 AM
Re: Applied Science Project Meeting Availability
To: Cole Lam, Philip A. Barber, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Siri Suggestion
1 contact and 1 event
Review

Hi Cole,

My apologies for the delay in messaging! I was on vacation and just returned last week.

To answer your questions:

1) Feel free to email at anytime, I do not mind- however, I am most likely to respond M-F between 9 and 6 pm.
2) Email works for me! As the year goes on, you may also text me (587-888-0687) if you'd like 🙂. If it is an urgent message, I will most likely respond faster on text.
3) I have no preference, but I think it would be good to meet weekly once we have your project started. I recently finished my undergraduate thesis, and I found it super helpful to have a set meeting time to ask questions!

Lastly, I can send out a zoom link for the friday meeting if Dr. Barber chooses online 🙂!

I'm super excited for you to join us officially!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

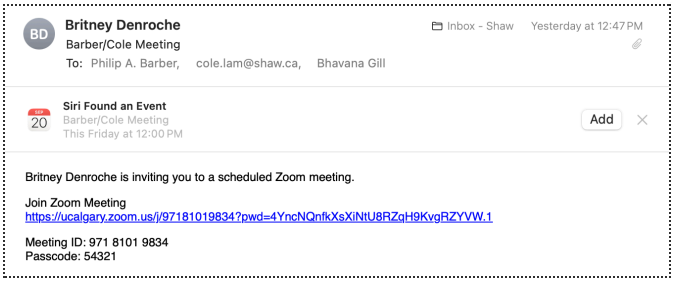
Lastly, I continued reading *A Classification and Outline of Cerebrovascular Diseases II*, although switched to reading *A longitudinal magnetic resonance imaging study of neurodegenerative and small vessel disease, and clinical cognitive trajectories in non demented patients with transient ischemic attack: the PREVENT study* (A longitudinal magnetic resonance imaging study of neurodegenerative and small vessel disease, and clinical cognitive trajectories in non demented patients with transient ischemic attack: the PREVENT study), because I figured the other article would be better as reference material than for learning about the field.

September 17, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read the literature sent by Dr. Barber	None	1. Read ~1 article/2 days

Review

This day, Britney sent me the zoom link for our meeting on Friday.



Britney Denroche Inbox - Shaw Yesterday at 12:47 PM
Barber/Cole Meeting
To: Philip A. Barber, cole.lam@shaw.ca, Bhavana Gill

Siri Found an Event
Barber/Cole Meeting
This Friday at 12:00 PM
Add

Britney Denroche is inviting you to a scheduled Zoom meeting.

Join Zoom Meeting
https://ucalgary.zoom.us/j/97181019834?pwd=4YncNQnfkXsXiNtU8RZqH9KvgRZYVW.1

Meeting ID: 971 8101 9834
Passcode: 54321

September 18, 2024

Tasks To-do

- [ ] Read the literature sent by Dr. Barber

Tasks Completed

None

Review

During class, I finished reading *A longitudinal magnetic resonance imaging study of neurodegenerative and small vessel disease, and clinical cognitive trajectories in non demented patients with transient ischemic attack: the PREVENT study*.

Notes

1. Read ~1 article/2 days

September 20, 2024

Tasks To-do

- [ ] Read the literature sent by Dr. Barber
- [ ] Send completed UCID and Young Persons Accessing Laboratories Agreement forms to Dr. Barber (New)

Tasks Completed

None

Notes

1. Read ~1 article/2 days

Review

From 12:00 PM - 1:00 PM, I had my second meeting with Dr. Barber and Bhavana.
My prepared discussion questions were as follows:

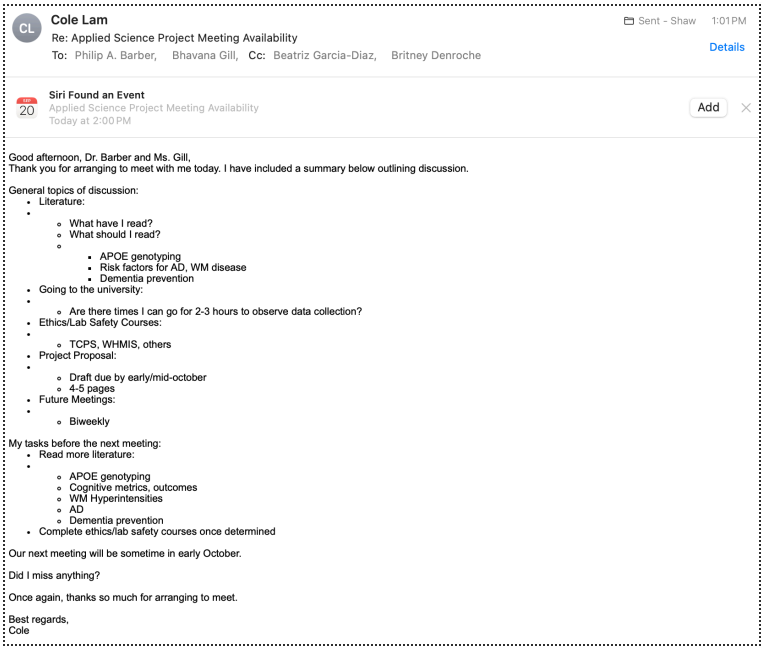
- [x] Can we create a proper schedule for meeting on a (relatively) weekly basis?
- [x] Is there any specific literature that you would like me to focus on, rather than everything?
- [x] Are there any ethics courses or the like that I need to take (or programming or statistics concepts)?
- [ ] Is there a general idea as to what my project will look like to begin working on a project proposal?
    - [ ] What is the general research question?
    - [x] What are the goals?
    - [x] Is there an idea of the kind of work I will be doing?

My meeting notes were as followed:

- The Project
    - Goals
        - Going to the university: going for 2-3 hour blocks
    - What kind of work?
        - A lot of the work is around detecting brain change, but also cognitive data
    - Project Proposal
        - Draft Proposal for mid-October
        - 4-5 pages
            - 1-2 pages background research
            - 0.5 page objective, hypothesis
            - Methods and everything else 1-2 pages

        - Paragraph on anticipated results (includes limitations)
        - Final paragraph: 2-3 sentences, impact
    - Methods: observing the techniques
        - APOE Genotyping (lab work)
- Literature/Courses
    - Literature:
        - APOE genotyping
        - PCR - Campbell Biology textbook
        - Cognitive metrics, outcomes
        - AD, SVD, vascular dementia
        - Biomarkers
        - WM hyperintensities
        - Vascular disease risk factors
        - Dementia prevention
    - Courses:
        - TPCS
        - WHMIS
- Logistics
    - Biweekly meetings

I then sent them a summary email with everything we discussed to confirm I didn't miss anything:



Cole Lam — Sent - Shaw 1:01PM

Re: Applied Science Project Meeting Availability

To: Philip A. Barber, Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche — Details

Siri Found an Event

Applied Science Project Meeting Availability

Today at 2:00 PM — Add

Good afternoon, Dr. Barber and Ms. Gill,
Thank you for arranging to meet with me today. I have included a summary below outlining discussion.

General topics of discussion:

- Literature:
    - What have I read?
    - What should I read?
        - APOE genotyping
        - Risk factors for AD, WM disease
        - Dementia prevention
- Going to the university:
    - Are there times I can go for 2-3 hours to observe data collection?
- Ethics/Lab Safety Courses:
    - TCPS, WHMIS, others
- Project Proposal:
    - Draft due by early/mid-october
    - 4-5 pages
- Future Meetings:
    - Biweekly

My tasks before the next meeting:

- Read more literature:
    - APOE genotyping
    - Cognitive metrics, outcomes
    - WM Hyperintensities
    - AD
    - Dementia prevention
- Complete ethics/lab safety courses once determined

Our next meeting will be sometime in early October.

Did I miss anything?

Once again, thanks so much for arranging to meet.

Best regards,
Cole

Then, I talked with Dr. Garcia about what occurred during the meeting, and also talked about getting a UCID for taking the ethics courses and going into the lab. I then sifted through the articles that Dr. Barber sent to find the ones that fit into the topics Dr. Barber told me to focus on. I then uploaded them all to PaperPile.
Later that evening, Dr. Garcia reminded Dr. Barber about completing UCID and Young Persons Accessing Laboratories Agreement forms that needed to be completed. Dr. Barber filled out his portion of the forms and sent them back to me.

September 22, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read the literature sent by Dr. Barber ☐ Send completed UCID and Young Persons Accessing Laboratories Agreement forms to Dr. Barber	None	1. Find APOE genotyping articles to read before other topics.

Review

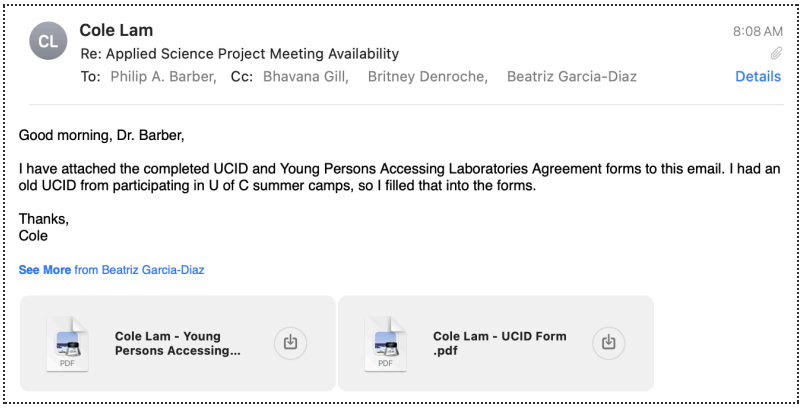
This day, I filled out all of the required forms, getting Dr. Garcia as a witness for my parents' signature. I prepared my email to send to Dr. Barber for Monday morning (so as to not bother him on the weekend).

September 23, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read into APOE genotyping (Edited)	☑ Send completed UCID and Young Persons Accessing Laboratories Agreement forms to Dr. Barber	1. Find APOE genotyping articles to read before other topics.

Review

This morning, I sent the completed forms back to Dr. Barber, and mentioned that while he had initially noted down getting a new UCID that I had one from the past to reactivate.



I also found some APOE genotyping articles that I could start reading for background research regarding the methods of this project, including APOE and dementia – resequencing and genotyping in 105,597 individuals. I also

started constructing my project proposal, beginning with my introduction. All of the content is rough, but my goal was to begin outlining the general idea of the project, using APOE genotyping for predicting white matter disease and transient ischemic attacks.

September 24, 2024

Tasks To-do

- [ ] Read into APOE genotyping

Tasks Completed

None

Review

During class, I began reading *Population-based blood screening for preclinical Alzheimer's disease in a British birth cohort at age 70* (Population-based blood screening for preclinical Alzheimer's disease in a British birth cohort at age 70). This was one of the few articles that Dr. Barber sent me that included APOE genotyping as a covariate.

Notes

None

September 26, 2024

Tasks To-do

- [ ] Read into APOE genotyping

Tasks Completed

None

Review

During class, because I gained access to some APOE genotype specific articles, I uploaded those to PaperPile and began reading one of them. This article is *APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches.* (APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches). I plan to email Dr. Barber and his assistants on Monday, September 30 with my progress in literature, and also to clarify the next meeting date.

Notes

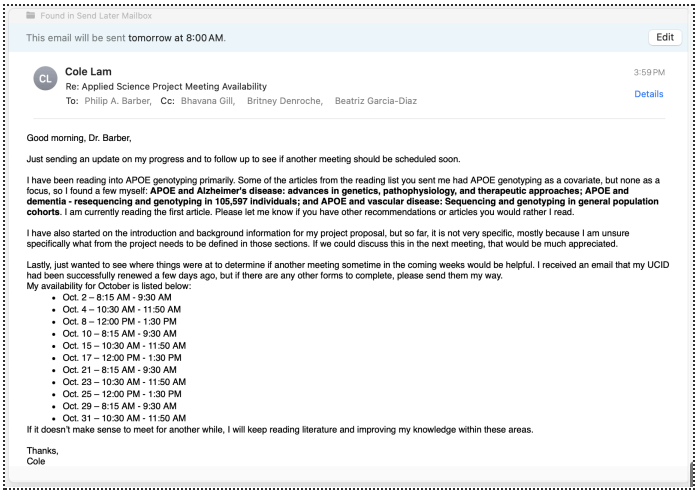
None

September 29, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read into APOE genotyping	None	None

Review

This day, I organized my logbook to be ready for submission the following day. I added all of my citations for my background research, and included all of the information I learned from it that I thought was important to note down. I also drafted my follow-up email for Dr. Barber and his assistants today and scheduled it for 8:00 AM the next day. It included information such as the literature I had been reading, my progress for the project proposal, that my UCID had been successfully renewed, and also potential meeting times for the future.



Found in Send Later Mailbox

This email will be sent tomorrow at 8:00 AM. Edit

CL **Cole Lam** 3:59 PM

Re: Applied Science Project Meeting Availability

To: Philip A. Barber, Cc: Bhavana Gill, Britney Denroche, Beatriz Garcia-Diaz Details

Good morning, Dr. Barber,

Just sending an update on my progress and to follow up to see if another meeting should be scheduled soon.

I have been reading into APOE genotyping primarily. Some of the articles from the reading list you sent me had APOE genotyping as a covariate, but none as a focus, so I found a few myself: **APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches; APOE and dementia - resequencing and genotyping in 105,597 individuals; and APOE and vascular disease: Sequencing and genotyping in general population cohorts**. I am currently reading the first article. Please let me know if you have other recommendations or articles you would rather I read.

I have also started on the introduction and background information for my project proposal, but so far, it is not very specific, mostly because I am unsure specifically what from the project needs to be defined in those sections. If we could discuss this in the next meeting, that would be much appreciated.

Lastly, just wanted to see where things were at to determine if another meeting sometime in the coming weeks would be helpful. I received an email that my UCID had been successfully renewed a few days ago, but if there are any other forms to complete, please send them my way.
My availability for October is listed below:

- Oct. 2 – 8:15 AM - 9:30 AM
- Oct. 4 – 10:30 AM - 11:50 AM
- Oct. 8 – 12:00 PM - 1:30 PM
- Oct. 10 – 8:15 AM - 9:30 AM
- Oct. 15 – 10:30 AM - 11:50 AM
- Oct. 17 – 12:00 PM - 1:30 PM
- Oct. 21 – 8:15 AM - 9:30 AM
- Oct. 23 – 10:30 AM - 11:50 AM
- Oct. 25 – 12:00 PM - 1:30 PM
- Oct. 29 – 8:15 AM - 9:30 AM
- Oct. 31 – 10:30 AM - 11:50 AM

If it doesn't make sense to meet for another while, I will keep reading literature and improving my knowledge within these areas.

Thanks,
Cole

September 30, 2024

Tasks To-do

- [ ] Read into APOE genotyping
- [ ] Confirm that my weekly email was successfully sent (New)

Tasks Completed

- [x] Confirm that my weekly email was successfully sent (New)

Review

During class, I spent time organizing my logbook's Background Research section, and then continued reading into APOE and the APOE genotype. I was reading *APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches* when I realized that while I was reading about the APOE genotype and its impact on the brain, I did not know what the APOE genotype and the proteins were normally responsible for doing. To help with that, I found a site that talked about the function of the APOE genotype (APOE gene: MedlinePlus Genetics), where I noted down what the APOE gene was responsible for. It also appeared that my email drafted that day before didn't send, so I created a reminder to resend the email at home, because my personal email doesn't load on Webber property.

Notes

1. I need to understand what the APOE proteins do before I can properly understand how it is associated with late-onset AD.

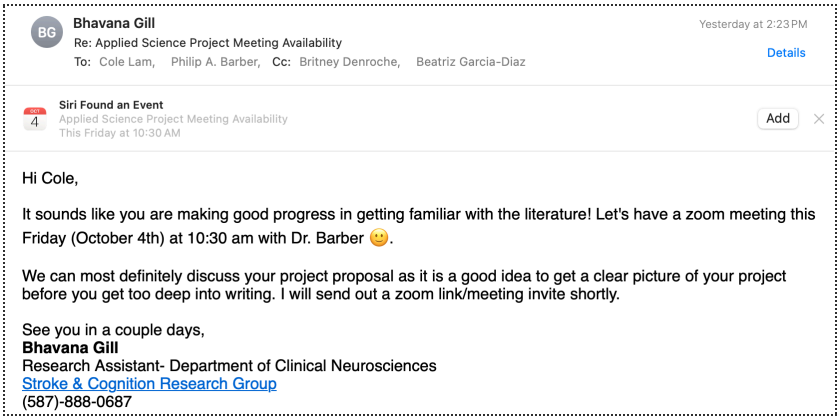
Daily Notes

October 1, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read into APOE genotyping	None	None

Review

This day, Bhavana responded to my biweekly update email, providing a date (10:30 AM, Friday, October 4, 2024). She mentioned that the goal of the meeting would be to establish what my project will look like so I can begin drafting my project proposal efficiently.



Bhavana Gill Yesterday at 2:23 PM
Re: Applied Science Project Meeting Availability
To: Cole Lam, Philip A. Barber, Cc: Britney Denroche, Beatriz Garcia-Diaz
Details

Siri Found an Event
Applied Science Project Meeting Availability
This Friday at 10:30 AM
Add

Hi Cole,

It sounds like you are making good progress in getting familiar with the literature! Let's have a zoom meeting this Friday (October 4th) at 10:30 am with Dr. Barber 🙂.

We can most definitely discuss your project proposal as it is a good idea to get a clear picture of your project before you get too deep into writing. I will send out a zoom link/meeting invite shortly.

See you in a couple days,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

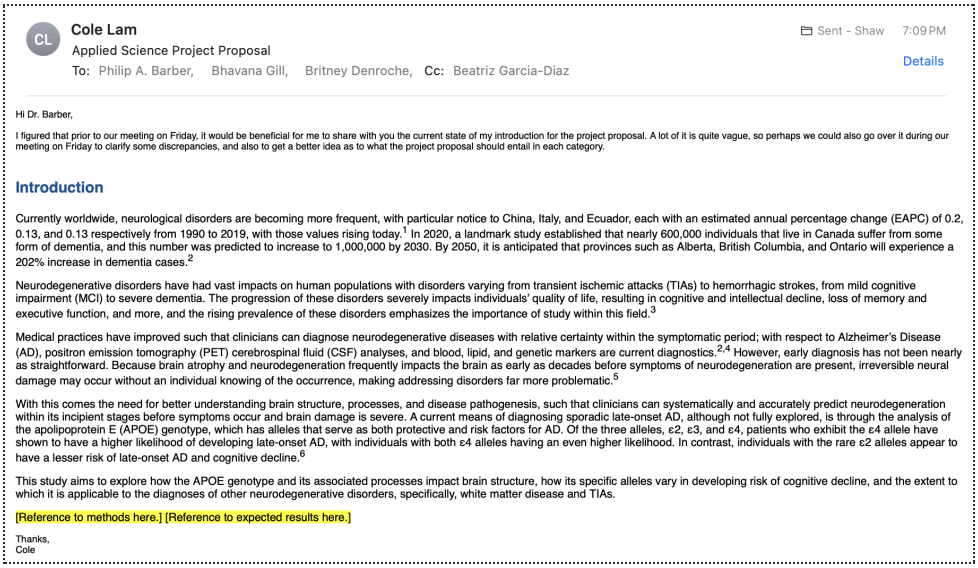
October 2, 2024

Tasks To-do	Tasks Completed	Notes
☐ Read into APOE genotyping ☐ Finish the introduction for the project proposal and send to Dr. Barber (New)	☑ Finish the introduction for the project proposal and send to Dr. Barber (New)	None

Review

In class, we covered the major mistakes that people made in their September logbooks: schedules are too general, daily notes are too short and vague, background research uses internet websites more than scientific literature, etc. Following this, I continued drafting my project proposal (Cole Lam - ASP Project Proposal), specifically in the background research section. After that, I had a meeting with Dr. Garcia talking about the plans for the Friday

meeting. She told me that I should try and send my project proposal introduction ahead of time, and then push for information about the research question, short and long term goals, perhaps some methods, and then another meeting date for the future. That evening, I finished my first draft for the introduction for the project proposal, and sent that to Dr. Barber.



CL **Cole Lam** — Sent - Shaw 7:09 PM

Applied Science Project Proposal

To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz — Details

Hi Dr. Barber,

I figured that prior to our meeting on Friday, it would be beneficial for me to share with you the current state of my introduction for the project proposal. A lot of it is quite vague, so perhaps we could also go over it during our meeting on Friday to clarify some discrepancies, and also to get a better idea as to what the project proposal should entail in each category.

Introduction

Currently worldwide, neurological disorders are becoming more frequent, with particular notice to China, Italy, and Ecuador, each with an estimated annual percentage change (EAPC) of 0.2, 0.13, and 0.13 respectively from 1990 to 2019, with those values rising today.[1] In 2020, a landmark study established that nearly 600,000 individuals that live in Canada suffer from some form of dementia, and this number was predicted to increase to 1,000,000 by 2030. By 2050, it is anticipated that provinces such as Alberta, British Columbia, and Ontario will experience a 202% increase in dementia cases.[2]

Neurodegenerative disorders have had vast impacts on human populations with disorders varying from transient ischemic attacks (TIAs) to hemorrhagic strokes, from mild cognitive impairment (MCI) to severe dementia. The progression of these disorders severely impacts individuals' quality of life, resulting in cognitive and intellectual decline, loss of memory and executive function, and more, and the rising prevalence of these disorders emphasizes the importance of study within this field.[3]

Medical practices have improved such that clinicians can diagnose neurodegenerative diseases with relative certainty within the symptomatic period; with respect to Alzheimer's Disease (AD), positron emission tomography (PET) cerebrospinal fluid (CSF) analyses, and blood, lipid, and genetic markers are current diagnostics.[2,4] However, early diagnosis has not been nearly as straightforward. Because brain atrophy and neurodegeneration frequently impacts the brain as early as decades before symptoms of neurodegeneration are present, irreversible neural damage may occur without an individual knowing of the occurrence, making addressing disorders far more problematic.[5]

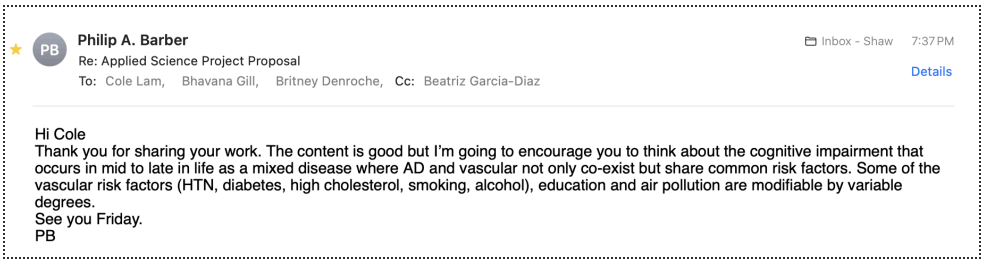
With this comes the need for better understanding brain structure, processes, and disease pathogenesis, such that clinicians can systematically and accurately predict neurodegeneration within its incipient stages before symptoms occur and brain damage is severe. A current means of diagnosing sporadic late-onset AD, although not fully explored, is through the analysis of the apolipoprotein E (APOE) genotype, which has alleles that serve as both protective and risk factors for AD. Of the three alleles, ε2, ε3, and ε4, patients who exhibit the ε4 allele have shown to have a higher likelihood of developing late-onset AD, with individuals with both ε4 alleles having an even higher likelihood. In contrast, individuals with the rare ε2 alleles appear to have a lesser risk of late-onset AD and cognitive decline.[6]

This study aims to explore how the APOE genotype and its associated processes impact brain structure, how its specific alleles vary in developing risk of cognitive decline, and the extent to which it is applicable to the diagnoses of other neurodegenerative disorders, specifically, white matter disease and TIAs.

[Reference to methods here.] [Reference to expected results here.]

Thanks,
Cole

Dr. Barber responded by saying the content was good, but to put more focus on neurodegeneration as part of mixed disease with vascular dementia as well, with risk factors such as hypertension, high cholesterol, diabetes, etc.



PB **Philip A. Barber** — Inbox - Shaw 7:37 PM

Re: Applied Science Project Proposal

To: Cole Lam, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz — Details

Hi Cole
Thank you for sharing your work. The content is good but I'm going to encourage you to think about the cognitive impairment that occurs in mid to late in life as a mixed disease where AD and vascular not only co-exist but share common risk factors. Some of the vascular risk factors (HTN, diabetes, high cholesterol, smoking, alcohol), education and air pollution are modifiable by variable degrees.
See you Friday.
PB

October 3, 2024

Tasks To-do

- ☐ Read into APOE genotyping
- ☐ Finish introduction of project proposal for Monday (New)

Tasks Completed

None

Review

This evening, I spent quite some time updating my logbook, modifying my introduction for the project proposal, and doing background research into the role of APOE on MVAD. As Dr. Garcia was adding suggestions into my logbook, I made modifications where appropriate, by making my logbook calendar more specific, adding some extra details to some of my daily entries, and fixing my citation page using Paperpile. I also made modifications to my project proposal, modifying the background information to relate to mixed dementia instead of strictly

Notes

1. Remember to make the calendar more comprehensive, with details for what I do each class/day, and also include as many tentative deadlines as possible.

	neurodegeneration. I included the information that Dr. Barber mentioned (VRFs such as HTN and DM). Lastly, I continued my background research reading the article *Vascular Risk Factors: Imaging and Neuropathological Correlates* (Vascular Risk Factors: Imaging and Neuropathologic Correlates) to learn more about VRFs.	

October 4, 2024

Tasks To-do

- [ ] Finish first draft of project proposal for Oct. 11 (New)
- [ ] Finish the TCPS2 CORE Course (New)
- [ ] Finish the CITI Course (New)
- [ ] Finish Lab Safety Course (New)
- [ ] Finish Biosafety Program (New)
- [ ] Finish Biosafety Bloodborne Pathogens Course (New)
- [ ] Create UCalgary email address (New)
- [ ] Send UCalgary email address to Dr. Barber (New)

Tasks Completed

- [x] Finish introduction of project proposal for Monday
- [x] Read into APOE genotyping

Notes

1. Meeting with Dr. Barber at 10:30 AM today
2. Project proposal is to be 1 page, 3500 characters MAX

Review

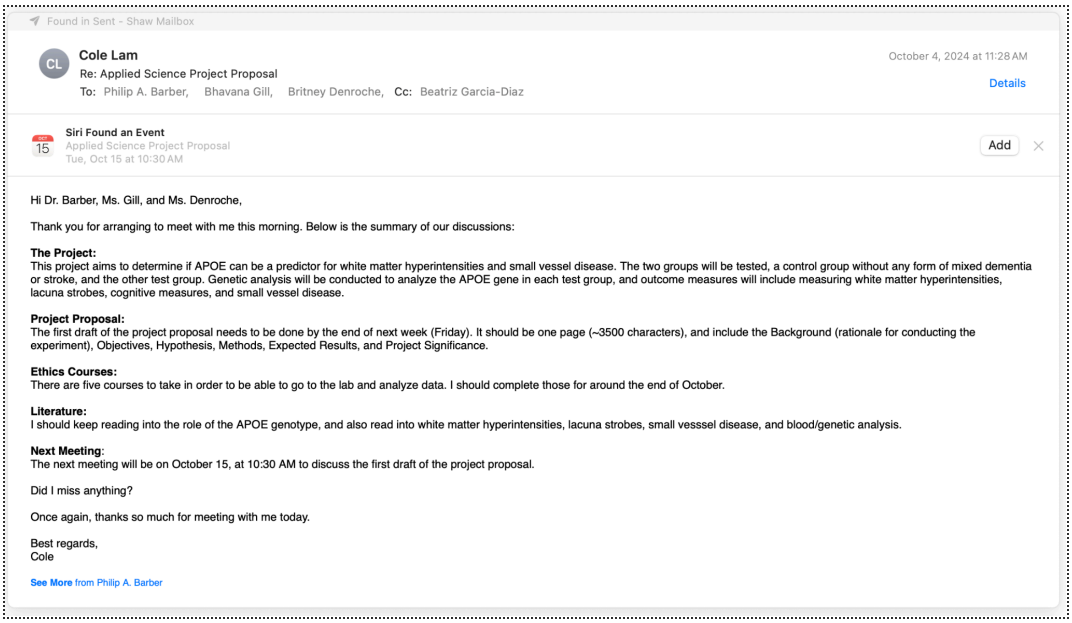
Today, before my meeting with Dr. Barber, I prepared all of my literature and documents to talk with Dr. Barber. I also organized my questions in order to be ready to talk to Dr. Barber.

Notes:

- The Project
    - My understanding: APOE genotype to understand brain structure and its impact on mixed dementia
    - Actual project:
        - APOE can be a predictor for white matter hyperintensities
            - Maybe microstructure
        - Observing cognitive outcomes/neuropsychological endpoint
        - Controls:
            - Is APOE genotype related to TIAs?
            - How does it relate to white matter hyperintensities?
    - APOE:
        - E4 is important for AD
        - Also associated with white matter hyperintensities
        - E3 allele is protective for AD
        - E2 allele vascular risk
        - So APOE isn't just a risk factor for only AD, but is also associated with other diseases, like white matter hyperintensities, genetics, and is associated with vascular risk factors
- Project Proposal: Due end of next week (one page total) (3500 characters) Final paper is 10-11 pages

double spaced
    - Introduction:
    - Background Research: rationale for doing this - short paragraph
    - Hypothesis: APOE genetic susceptibility is greater in TIA and is related to increased small vessel disease
    - Goals:
        - Observes frequency of APOE with different alleles with regard to TIAs
        - How APOE relates to white matter hyperintensities and small vessel diseases
        - How APOE relates to cognitive outcomes/decline
    - Methods: Describe the
        - Longitudinal study
        - Lines about APOE genotyping → genetic analysis
        - Outcome measures: measuring white matter hyperintensities, cognitive measures, small vessel disease
        - Control: individuals without TIAs/small vessel disease
        - Observe in two groups
        - Lacuna Strobes and white matter hyperintensities are forms of small vessel disease
            - Quantitate
    - Conclusion (3-4 sentences MAX):
        - How does this all relate to cognitive decline?
        - Why is this important?
            - Determining cognitive/genetic susceptibility is important because its non modifiable
        - Expected results (1-2 sentences)
        - Extension: Does modifying VRFs have the potential to impact genetic susceptibility?
- Ethics Courses
    - Bhavana finished organizing all the courses for blood work, ethics, etc.
        - Two primary courses for going into the lab, and three courses specific for blood work
    - Finish the courses by:
    - Get an idea of latin
    - Need these course to access the data
- Going to the University
- Next Meeting
    - October 15, 10:30 - 11:30 AM

I then sent a summary email about the topics that we discussed, and Dr. Barber confirmed that I didn't miss any details.



Found in Sent - Shaw Mailbox

Cole Lam
Re: Applied Science Project Proposal
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
October 4, 2024 at 11:28 AM
Details

Siri Found an Event
Applied Science Project Proposal
Tue, Oct 15 at 10:30 AM
Add

Hi Dr. Barber, Ms. Gill, and Ms. Denroche,

Thank you for arranging to meet with me this morning. Below is the summary of our discussions:

The Project:
This project aims to determine if APOE can be a predictor for white matter hyperintensities and small vessel disease. The two groups will be tested, a control group without any form of mixed dementia or stroke, and the other test group. Genetic analysis will be conducted to analyze the APOE gene in each test group, and outcome measures will include measuring white matter hyperintensities, lacuna strobes, cognitive measures, and small vessel disease.

Project Proposal:
The first draft of the project proposal needs to be done by the end of next week (Friday). It should be one page (~3500 characters), and include the Background (rationale for conducting the experiment), Objectives, Hypothesis, Methods, Expected Results, and Project Significance.

Ethics Courses:
There are five courses to take in order to be able to go to the lab and analyze data. I should complete those for around the end of October.

Literature:
I should keep reading into the role of the APOE genotype, and also read into white matter hyperintensities, lacuna strobes, small vesssel disease, and blood/genetic analysis.

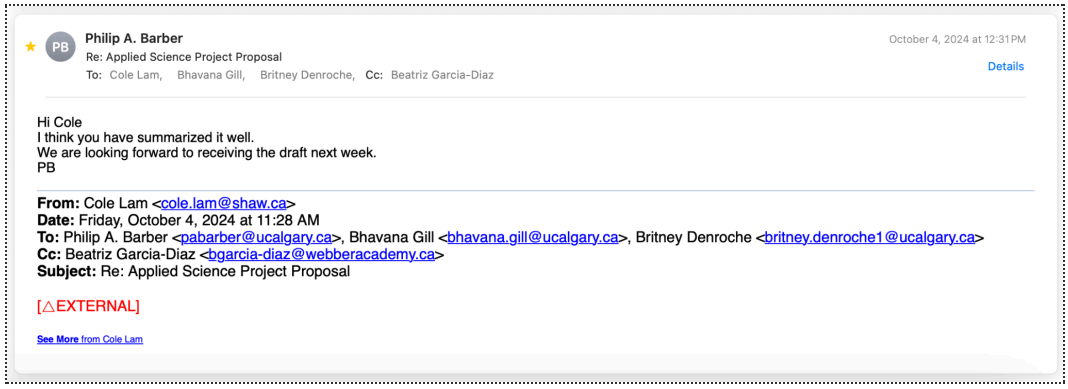
Next Meeting:
The next meeting will be on October 15, at 10:30 AM to discuss the first draft of the project proposal.

Did I miss anything?

Once again, thanks so much for meeting with me today.

Best regards,
Cole

See More from Philip A. Barber



Philip A. Barber
Re: Applied Science Project Proposal
To: Cole Lam, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
October 4, 2024 at 12:31 PM
Details

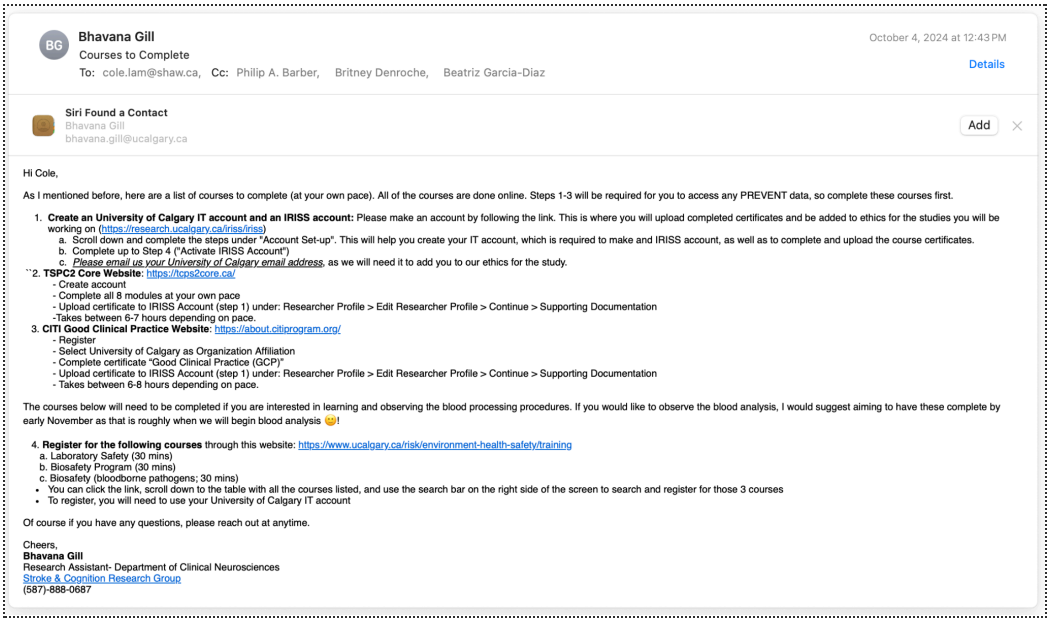
Hi Cole
I think you have summarized it well.
We are looking forward to receiving the draft next week.
PB

From: Cole Lam <cole.lam@shaw.ca>
Date: Friday, October 4, 2024 at 11:28 AM
To: Philip A. Barber <pabarber@ucalgary.ca>, Bhavana Gill <bhavana.gill@ucalgary.ca>, Britney Denroche <britney.denroche1@ucalgary.ca>
Cc: Beatriz Garcia-Diaz <bgarcia-diaz@webberacademy.ca>
Subject: Re: Applied Science Project Proposal

[△EXTERNAL]

See More from Cole Lam

Bhavana also sent me the list of courses to complete. She mentioned that I need to create a UCalgary email account in order to register for most of the courses, and that I should send it to them once I have done so.



Bhavana Gill
Courses to Complete
To: cole.lam@shaw.ca, Cc: Philip A. Barber, Britney Denroche, Beatriz Garcia-Diaz
October 4, 2024 at 12:43 PM
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

As I mentioned before, here are a list of courses to complete (at your own pace). All of the courses are done online. Steps 1-3 will be required for you to access any PREVENT data, so complete these courses first.

1. **Create an University of Calgary IT account and an IRISS account:** Please make an account by following the link. This is where you will upload completed certificates and be added to ethics for the studies you will be working on (https://research.ucalgary.ca/iriss/iriss)
   a. Scroll down and complete the steps under "Account Set-up". This will help you create your IT account, which is required to make and IRISS account, as well as to complete and upload the course certificates.
   b. Complete up to Step 4 ("Activate IRISS Account")
   c. *Please email us your University of Calgary email address*, as we will need it to add you to our ethics for the study.

``2. **TSPC2 Core Website**: https://tcps2core.ca/
- Create account
- Complete all 8 modules at your own pace
- Upload certificate to IRISS Account (step 1) under: Researcher Profile > Edit Researcher Profile > Continue > Supporting Documentation
-Takes between 6-7 hours depending on pace.

3. **CITI Good Clinical Practice Website**: https://about.citiprogram.org/
- Register
- Select University of Calgary as Organization Affiliation
- Complete certificate "Good Clinical Practice (GCP)"
- Upload certificate to IRISS Account (step 1) under: Researcher Profile > Edit Researcher Profile > Continue > Supporting Documentation
- Takes between 6-8 hours depending on pace.

The courses below will need to be completed if you are interested in learning and observing the blood processing procedures. If you would like to observe the blood analysis, I would suggest aiming to have these complete by early November as that is roughly when we will begin blood analysis 🙂!

4. **Register for the following courses** through this website: https://www.ucalgary.ca/risk/environment-health-safety/training
   a. Laboratory Safety (30 mins)
   b. Biosafety Program (30 mins)
   c. Biosafety (bloodborne pathogens; 30 mins)
- You can click the link, scroll down to the table with all the courses listed, and use the search bar on the right side of the screen to search and register for those 3 courses
- To register, you will need to use your University of Calgary IT account

Of course if you have any questions, please reach out at anytime.

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

October 6, 2024

Tasks To-do

- [ ] Finish first draft of project proposal for Oct. 11
- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Send UCalgary email address to Dr. Barber

Tasks Completed

- [x] Create UCalgary email address

Review

This day, I did some definition research into small vessel disease, white matter hyperintensities, and mixed dementia. After this, I started drafting my new project proposal (Cole Lam - ASP Project Proposal) and completed my first draft for everything but expected results. I plan on asking Dr. Garcia on Tuesday how to differentiate the experiment hypothesis and expected results. (aren't they basically the same thing?) I then also created my UCalgary email address in order to be able to complete all of the required ethics courses (email address: cole.lam1@ucalgary.ca). I planned to send the email address to them on Monday morning.

Notes

1. Project proposal is to be 1 page, 3500 characters MAX

October 7, 2024

Tasks To-do

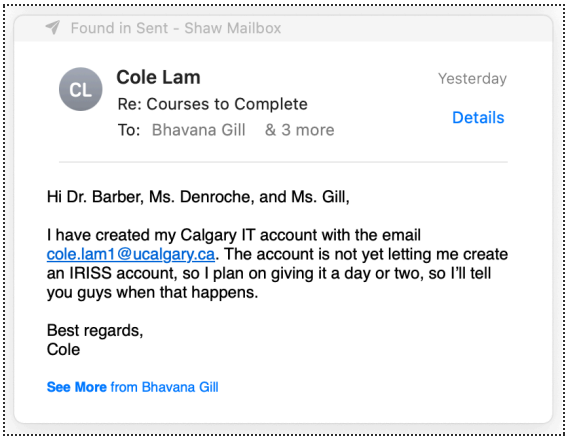
- [ ] Finish first draft of project proposal for Oct. 11
- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Create IRISS account (New)

Tasks Completed

- [x] Send UCalgary email address to Dr. Barber

Review

I sent my UCalgary email to Dr. Barber and his assistants, mentioning that the University isn't letting me create my IRISS account yet.



Found in Sent - Shaw Mailbox

CL **Cole Lam** Yesterday

Re: Courses to Complete

To: Bhavana Gill & 3 more Details

Hi Dr. Barber, Ms. Denroche, and Ms. Gill,

I have created my Calgary IT account with the email cole.lam1@ucalgary.ca. The account is not yet letting me create an IRISS account, so I plan on giving it a day or two, so I'll tell you guys when that happens.

Best regards,
Cole

See More from Bhavana Gill

Notes

None

October 8, 2024

Tasks To-do

- [ ] Refine first draft of project proposal for Oct. 11
- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Create IRISS account

Tasks Completed

- [x] Finish first draft of project proposal for Oct. 11

Review

In class, Dr. Garcia talked to us about the Webber Academy Internal Science Fair, and what plans we should have for making sure that we are ready. The internal fair is on March 11th, and for now, we should create a detailed plan for the coming months to make sure that all the SF deadlines are met. We also have to upload our projects to the CYSF online portal, and to make sure that we use content from our logbook into sections such as background research. The CYSF online portal closes on March 28th. Dr. Garcia also mentioned that we need to upload any ethics onto the CYSF online portal. Then, if we are within the top 15 projects in SH, the CYSF is on April 10-12. Then, Dr. Garcia talked about how to properly use Paperpile and how to change the citations style so that we don't have to manually input sources and make modifications to the citations. Then, for the rest of the class, I finished the first draft (unedited) of my project proposal and did some research into WMHs. I sent my current project proposal to Dr. Garcia to review (Cole Lam - ASP Project Proposal), who told me that because my project proposal is very short that I will have more work to write my paper at the end of the year. The most significant things that I learned were that WMHs are heritable, like the APOE gene, and that some studies have revealed that high cholesterol levels are one of the most significant risk factors for WMHs, which is what the APOE genotype is responsible for regulating. There may be an association there that could be used for predicting the relationship between APOE and WMHs.

Notes

1. Because I have old drafts of my project proposal introduction within the Google Doc back-ups, I can use those to help with the drafting of my introduction for the paper at the end of the year.

October 10, 2024

Tasks To-do

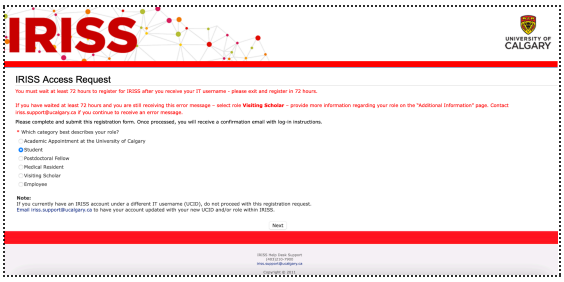
- [ ] Refine first draft of project proposal for Oct. 11
- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Create IRISS account

Tasks Completed

None

Review

This day, in class, I looked through the comments Dr. Garcia gave me for my one page project proposal. Specifically, I added details in the Background section outlining the project specifically, and added some more specificity for the Project Significance section, as well. (Cole Lam - ASP Project Proposal) I also tried to create my IRISS account for doing the ethics courses, but my account is not yet letting me complete the form.



After this, I continued to read into WMHs and SVD; specifically, *What are White Matter Hyperintensities Made of? Relevance to Vascular Cognitive Impairment*.

October 11, 2024

Tasks To-do

- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Create IRISS account

Tasks Completed

- [x] Refine first draft of project proposal for Oct. 11

Notes

None

Review

This day, I sent my first draft of my project proposal to Dr. Barber. I also updated him that my IRISS account was not allowing me to complete my account registration, and that I had been reading literature on WMHs and CSVD. I also sent a few questions that I had about my project proposal.

October 13, 2024

Tasks To-do

- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Create IRISS account

Tasks Completed

None

Review

I started on my TCPS-2: CORE 2022 course, and completed modules A1-6. I took notes on the information within my background research section. The content included what privacy prospective research participants are entitled to, and what information they should be told, as well as what kinds of projects require ethics approval.

Notes

None

October 15, 2024

Tasks To-do

- [ ] Finish second draft of project proposal for Oct. 23 (New)
- [ ] Finish the TCPS2 CORE Course
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

- [x] Create IRISS account

Notes

1. Meeting with Dr. Barber at 10:30 AM
2. Oral presentation on November 4th

Review

In class, Dr. Garcia talked about what we should be doing this class and for the rest of the month. Specifically, that everyone needed to create their account for the CYSF portal, and then that we should start planning for the rest of the month for our project proposals, oral presentations, etc. She mentioned that we should email our mentors if we haven't contacted them in a while, but my meeting with them was today at 10:30 AM, so I emailed them afterward with a summary of our discussions (see below). Then, she went over the oral presentation and how we should plan to make sure it gets done. My oral presentation day is November 4. She also gave us helpful tips about how to structure our presentation (10 min content, 5 min questions), and how we should plan out our slideshow

presentation (10-15 slides). She also gave us our rubric (Research Proposal Oral Presentation Rubric). Then, I met with Dr. Barber about my first draft of the project proposal.
Notes:

- Project Proposal
    - Components:
        - Background
            - In this project, you will be acquiring data from the PREVENT study which is a …
        - Objectives
            - Relationship APOE E4 alleles status with homozygous/heterozygous vs E2 with WMH volume (specify in TIA patients vs healthy controls)
            - Does APOE convey risk to anything related to CSVD and WMHs?
        - Alternate/Null Hypothesis
            - Only alternate hypothesis (no need for a null hypothesis)
            - Will address the hypothesis by proposing these three objectives
        - Methodology (be more specific)
            - Outcomes (only 2)
                - Include a link between APOE and WMHs (with a reference)
                - WHMs using MRIS
                - CVSD scores
            - Clinical outcome (not mixed dementia):
                - Cognitive decline
            - APOE genotype by PCR analysis
            - How will we analyze the data? (descriptive statistics)
                - For more complex analysis: potential confounding factors in the analysis (age, risk factors)
                - Objective: relationship between APOE (nonmodifiable) and vascular risk factors (modifiable) (are vascular risk factors less modifiable with genetic factors)
                - Multi-linear regression models
                - Test objectives (APOE vs. WMHs/SVD → cognitive decline) adjusting for common covariates (VRFs and age)
            - Link TIA with cognitive decline
- Ethics Courses
    - Progress:
        - Nearly done the TCPS2
        - IRISS account request is pending
- Next Meeting
    - October 23, 10:30 AM
- Other
    - Send proposal through Microsoft OneDrive

Britney also sent me the study protocol for the PREVENT study (PREVENT Study Protocol) along with an article that I could read to help me gain a better knowledge within this particular study (A longitudinal magnetic resonance imaging study of neurodegenerative and small vessel disease, and clinical cognitive trajectories in non demented patients with transient ischemic attack: the PREVENT study).
My summary email is below:

Cole Lam 11:17 AM
Re: Applied Science Project Proposal
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Siri Found an Event
Applied Science Project Proposal
Wed, Oct 23 at 10:30 AM
Add

Hi Dr. Barber, Ms. Gill, and Ms. Denroche,

Thank you so much for meeting with me today. The clarification for the project was really helpful in me understanding what is being conducted within this study.

Here is a summary of our discussions today:

Project Proposal:
The impact of the project, which was I had initially put down as mixed dementia, should be broadened to cognitive decline so the results of the study can be more impactful (mixed dementia may only develop in a few individuals within the sample). The background research section needs to be more specific in how the APOE genotype relates to WMHs, and should refer to cognitive decline and not mixed dementia. Only the alternate hypothesis is necessary (not the null hypothesis). The methodology section needs to be more specific, particularly with regard to the sample being studied, the descriptive statistics, etc. The study protocol has all of the methodology specifics for me to use for my proposal. The methods and study population should be of greatest focus in my edits.

Unfortunately, my Microsoft account is requiring that I confirm my account through my phone, which I don't have access to during school hours, so I will send the Microsoft Word document for my project proposal tonight.

Next Meeting:
Our next meeting will be on October 23, at 10:30 AM.

Did I miss anything?

Best regards,
Cole

This day, my IRISS account, after pending for many, many days, was finally approved. I shared this with Dr. Barber when emailing him my project proposal via Word document.

IRISSDoNotReply@ucalgary.ca Inbox - Exchange October 15, 2024 at 10:19 AM
Notice of IRISS Account Creation
To: cole.lam1@ucalgary.ca,
Reply-To: IRISSDoNotReply@ucalgary.ca

UNIVERSITY OF CALGARY

Dear Cole Lam,

An account has been created for you in IRISS. Follow these instructions to access your personal home page:

1. Click the link below.
2. You will be momentarily directed to the U of C Access page.
3. Enter your username and password just as you would if you were signing into My UofC.
4. You will land on your Personal Page.

Click HERE to go to IRISS now, or visit www.ucalgary.ca/iriss and follow the signs to log-in.

Cole Lam October 15, 2024 at 4:46 PM
Re: Applied Science Project Proposal
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Good afternoon, Dr. Barber, Ms. Gill, and Ms. Denroche,

I have converted my Google Doc project proposal to a Microsoft Word document, uploaded it to Onedrive and shared it with you: https://uofc-my.sharepoint.com/:w:/g/personal/cole_lam1_ucalgary_ca/Ee5vqShO4pxNs755HP1ZDJMBeWr0S7Im2rn1V1EYyXnWKw?e=HwjP8G
Please let me know if you cannot access it.

On a separate note, my IRISS account was activated about an hour ago, so if there was anything you need me to do now that the account is activated (other than uploading ethics course certificates), I can do that now.

Best regards,
Cole

October 17, 2024

Tasks To-do	Tasks Completed	Notes
☐ Finish second draft of project proposal for Oct. 23 ☐ Finish the CITI Course ☐ Finish Lab Safety Course ☐ Finish Biosafety Program ☐ Finish Biosafety Bloodborne Pathogens Course	☑ Finish the TCPS2 CORE Course	None

Review

This day, in class, we had a work block for our projects, when individual meetings were happening. I didn't have a meeting with Dr. Garcia, and I also wasn't meeting with Dr. Barber, so I was working on my project proposal. Specifically, I worked on modifying my background and objectives section of my project proposal to be more specific to my project, and to have a more broad impact using "cognitive decline" in place of "mixed dementia". I had hoped to also finish modifications to my methodology section, but because that will take a lot of time, I will make sure to work on it extra this weekend to make up for the lack of productivity.

In the evening, I finished Modules A7-9 for the TCPS 2: Core-2022 course and completed the final exam, passing, and receiving my certificate of completion. I then uploaded it to my IRISS account.


PANEL ON RESEARCH ETHICS
Navigating the ethics of human research

TCPS 2: CORE 2022

Certificate of Completion

This document certifies that

Cole Lam

successfully completed the Course on Research Ethics based on the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2: CORE 2022)

Certificate # 0001358818 **18 October, 2024**

October 20, 2024

Tasks To-do

- [ ] Finish second draft of project proposal for Oct. 23
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

None

Review

This evening, I created my account for my CITI GCP course, and completed the first module. I created notes under Background Research, including all relevant and important information. I then continued working on my project proposal, adding specificity to the Methodology section. Specifically, I added more information about the inclusion and exclusion criteria and the demographic for the study population.

Notes

None

October 21, 2024

Tasks To-do

- [ ] Finish second draft of project proposal for Oct. 23
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

None

Review

This class, Dr. Garcia spent some time talking to us about the oral presentations.
Notes:

- 10 minute speaking time
- Components:
  - Background
  - Research Question
  - Goals
  - Hypothesis
  - Methodology
    - Use a flow chart, not a paragraph of text
  - Significance
- Graphics are integral
  - Substitute text for graphics whenever is possible

Notes

None

October 22, 2024

Tasks To-do

- [ ] Finish second draft of project proposal for Oct. 23
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

None

Review

This evening, I continued making edits to my project proposal, and then sent an email to Dr. Barber and his assistants to let them know that my edits for the meeting the next day were finalized. My edits were specific to the Methodology section, and to the Project Significance section. I also added a long term goal to the proposal: to analyze how genetic risk factors impact the modifiability of vascular risk factors.

Notes

1. Meeting with Dr. Barber tomorrow at 10:30 AM.

October 23, 2024

Tasks To-do	Tasks Completed	Notes
☐ Finish third draft of project proposal for Oct. 26 (New) ☐ Finish the CITI Course ☐ Finish Lab Safety Course ☐ Finish Biosafety Program ☐ Finish Biosafety Bloodborne Pathogens Course	☑ Finish second draft of project proposal for Oct. 23	1. Meeting with Dr. Barber at 10:30 AM

Review

In this class, Dr. Garcia was talking about oral presentations and the kinds of structure that it needs and the components required to receive full marks. This included the background information, research question, short and long term objectives, hypothesis, methods, expected results, etc. Then, I went to my meeting with Dr. Barber, where we talked about my project proposal and areas to work on.

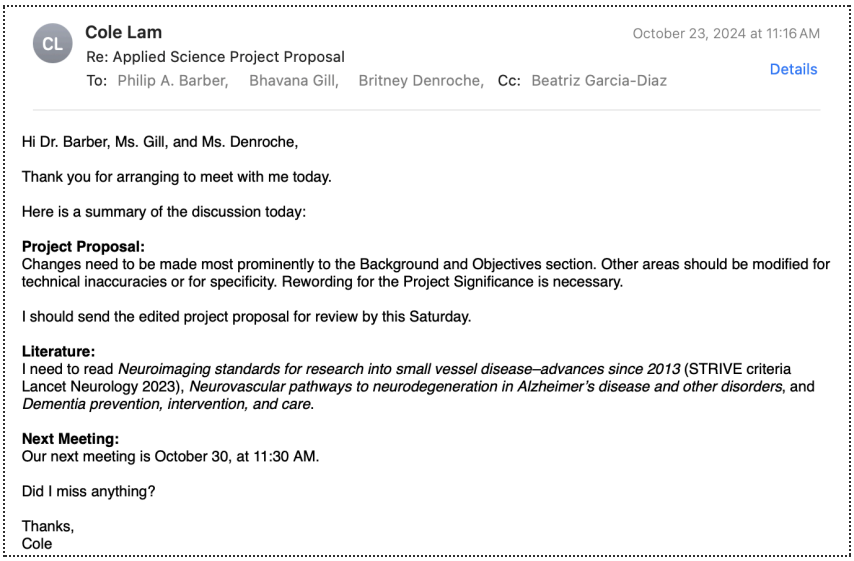
Notes:

- Project Proposal
    - Components:
        - Background
            - It needs to be written in simple 10th grade English, and as if the reader doesn't have any background knowledge within the area.
            - It should have a logical flow, leading from mixed disease to my project study and why it is designed the way it is.
            - "This is what mixed dementia is. AD and CSVD coexist as part of mixed dementia. The development of mixed dementia is often the result of modifiable risk factors, which provide an opportunity for disease prevention. The two-hit hypothesis tells us how AD-type diseases develop: genetic risk factors and vascular risk factors. CSVD is a vascular risk factor, and can be observed via MRI scans for WMHs. This is what WMHs are. APOE ε4 allele is a genetic risk factor for AD. Given this, my project aims to determine an association between AD so that genetic risk factors may help predict disease prevention with an association with vascular risk factors."
        - Objectives
            - Watch out for inaccuracies
            - Start with the hypothesis
            - WMHs are helping to determine associations with
        - Hypothesis
            - Generalize it to look at the impact of APOE on CSVD, not WMH, which can be used to determine CSVD.
        - Methodology
            - Modify the sample size, and note that it is a baseline, because the study may lose participants across the five-year span
            - Add mixed effects models to the list of statistical analyses
        - Literature:
            - Zlokovic, B. V. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders. Nat. Rev. Neurosci. 12 , 723–738 (2011).
            - Livingston, G. et al. Dementia prevention, intervention, and care. Lancet 390 ,

2673–2734 (2017).

- Science Fair Ethics:
    - My project is low risk.
- Next Meeting
    - Wednesday, October 30, 2024, at 11:30 AM.

After the meeting was over, I sent a summary email outlining everything from the meeting.



Cole Lam October 23, 2024 at 11:16 AM
Re: Applied Science Project Proposal
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Hi Dr. Barber, Ms. Gill, and Ms. Denroche,

Thank you for arranging to meet with me today.

Here is a summary of the discussion today:

Project Proposal:
Changes need to be made most prominently to the Background and Objectives section. Other areas should be modified for technical inaccuracies or for specificity. Rewording for the Project Significance is necessary.

I should send the edited project proposal for review by this Saturday.

Literature:
I need to read *Neuroimaging standards for research into small vessel disease–advances since 2013* (STRIVE criteria Lancet Neurology 2023), *Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders*, and *Dementia prevention, intervention, and care.*

Next Meeting:
Our next meeting is October 30, at 11:30 AM.

Did I miss anything?

Thanks,
Cole

The same evening, I worked on my project proposal, making edits to the background research section.

October 24, 2024

Tasks To-do	Tasks Completed	Notes
☐ Finish third draft of project proposal for Oct. 26 ☐ Finish the CITI Course ☐ Finish Lab Safety Course ☐ Finish Biosafety Program ☐ Finish Biosafety Bloodborne Pathogens Course	None	1. Project Proposal due October 31

Review

This day, I continued working on my project proposal, making overall changes to everything. My main focus was improving upon the Methodology section, in order to be more specific and avoid technical inaccuracies. I also generated a few questions for my proposal, so I sent them to Britney and Bhavana.

Cole Lam October 24, 2024 at 9:58 AM
Re: Applied Science Project Proposal
To: Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Good morning, Ms. Gill and Ms. Denroche,

I was making edits to my project proposal yesterday, and I came up with a few questions that I think could help me ensure scientific accuracy in my proposal. It would be great if you could address some of my questions to help me with my proposal! Thank you!

1. I'm assuming mixed disease, mixed dementia, and mixed brain pathologies are not interchangeable vocabulary. Could you please help me establish an understanding of what mixed disease is, compared to the others, because my searches online have only yielded results for mixed connective tissue disease?
2. Dr. Barber mentioned yesterday that the study had a baseline of 523 patients, although in the 2017 methods study, it indicated a total of 440 participants. Because I could not find the 523 number anywhere, could you perhaps tell me what the ratio of TIA patients to control patients are for my methodology section?
3. I wanted to confirm that outcome measures are different from outcomes. Outcomes measures refer to what you are measuring, and outcomes refer to what your outcome measures are hoping to draw conclusions about?
4. Are there any distinctions necessary between my hypothesis and expected results? Currently, my expected results and hypothesis are very similar and quite redundant.

Thank you so much!

Best regards,
Cole

I also sent my project proposal to Dr. Garcia to see if she could review it for my submission on Saturday.

Cole Lam October 24, 2024 at 3:21 PM
ASP Project Proposal
To: Beatriz Garcia-Diaz

Hi Dr. Garcia,

Dr. Barber requested that I send my final project proposal to him for Saturday, so I was wondering if you could review it and provide some potential changes to it for before then. If so, that would be so much appreciated!

Currently, my doc is in the form of a Microsoft Word document, so if you have a Microsoft account, I can add you directly to the actual document. Otherwise, I've attached a Google Doc equivalent.
(https://docs.google.com/document/d/1eBekm7xgLk4kyTpcuVpT5jJF6rIXURijz-HMAha84YQ/edit?tab=t.0)

Thanks,
Cole

Beatriz Garcia-Diaz October 24, 2024 at 6:17 PM
Re: ASP Project Proposal
To: Cole Lam

I'll try to review this by tomorrow's class but with gene club tonight and a few other proposal to review I won't get to it until tomorrow morning. Luckily your paper is short.
Cheers,
Dr. Garcia

See More from Cole Lam

--
Beatriz Garcia-Diaz, PhD
Science Lab Coordinator
Webber Academy
1515 - 93rd Street, S.W.
Calgary, Alberta T3H 4A8
Phone: (403) 277-4700 ext. 342

Cole Lam October 24, 2024 at 6:18 PM
Re: ASP Project Proposal
To: Beatriz Garcia-Diaz

Thank you so much! There is no rush.

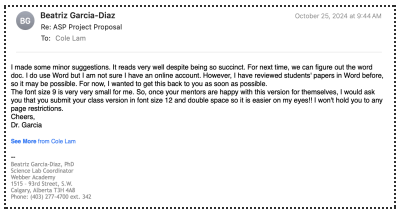
Best regards,
Cole

October 25, 2024

Tasks To-do	Tasks Completed	Notes
☐ Finish third draft of project proposal for Oct. 26 ☐ Finish the CITI Course ☐ Finish Lab Safety Course ☐ Finish Biosafety Program ☐ Finish Biosafety Bloodborne Pathogens Course	None	1. Project Proposal due October 31

Review

This morning, Dr. Garcia sent me some edits, so during the ASP class, I went through her comments and made changes accordingly. My own edits were to the Project Significance and Expected Results to become more concise. In class, I continued making those edits, and Dr. Garcia moved the oral presentations back, so my new presentation date is November 8.



Beatriz Garcia-Diaz
October 25, 2024 at 9:44 AM
Re: ASP Project Proposal
To: Cole Lam

I made some minor suggestions. It reads very well despite being so succinct. For next time, we can figure out the word doc. I do use Word but I am not sure I have an online account. However, I have reviewed students' papers in Word before, so it may be possible. For now, I wanted to get this back to you as soon as possible.
The font size 9 is very very small for me. So, once your mentors are happy with this version for themselves, I would ask you that you submit your class version in font size 12 and double space so it is easier on my eyes!! I won't hold you to any page restrictions.
Cheers,
Dr. Garcia

See More from Cole Lam

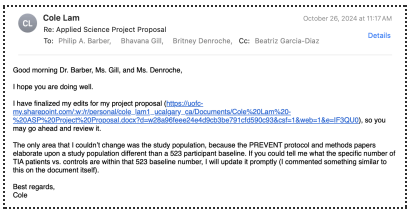
Beatriz Garcia-Diaz, PhD
Science Lab Coordinator
Webber Academy
1515 - 93rd Street, S.W.
Calgary, Alberta T3H 4A8
Phone: (403) 277-4700 ext. 342

October 26, 2024

Tasks To-do	Tasks Completed	Notes
☐ Finish the CITI Course ☐ Finish Lab Safety Course ☐ Finish Biosafety Program ☐ Finish Biosafety Bloodborne Pathogens Course	☑ Finish third draft of project proposal for Oct. 26	1. Project Proposal due October 31

Review

This morning, I made last edits to my project proposal, generalizing the information about WMHs to be about all the markers that are used for determining CSVD sum scores.



Cole Lam
October 26, 2024 at 11:17 AM
Re: Applied Science Project Proposal
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Good morning Dr. Barber, Ms. Gill, and Ms. Denroche,

I hope you are doing well.

I have finalized my edits for my project proposal (https://ucfc-my.sharepoint.com/:w:/r/personal/cole_lam1_ucalgary_ca/Documents/Cole%20Lam%20-%20ASP%20Project%20Proposal.docx?d=w09a96feee24e4d8cb3be791cfd590c93&csf=1&web=1&e=IF3QU0), so you may go ahead and review it.

The only area that I couldn't change was the study population, because the PREVENT protocol and methods papers elaborate upon a study population different than a 523 participant baseline. If you could tell me what the specific number of TIA patients vs. controls are within that 523 baseline number, I will update it promptly (I commented something similar to this on the document itself).

Best regards,
Cole

October 27, 2024

Tasks To-do

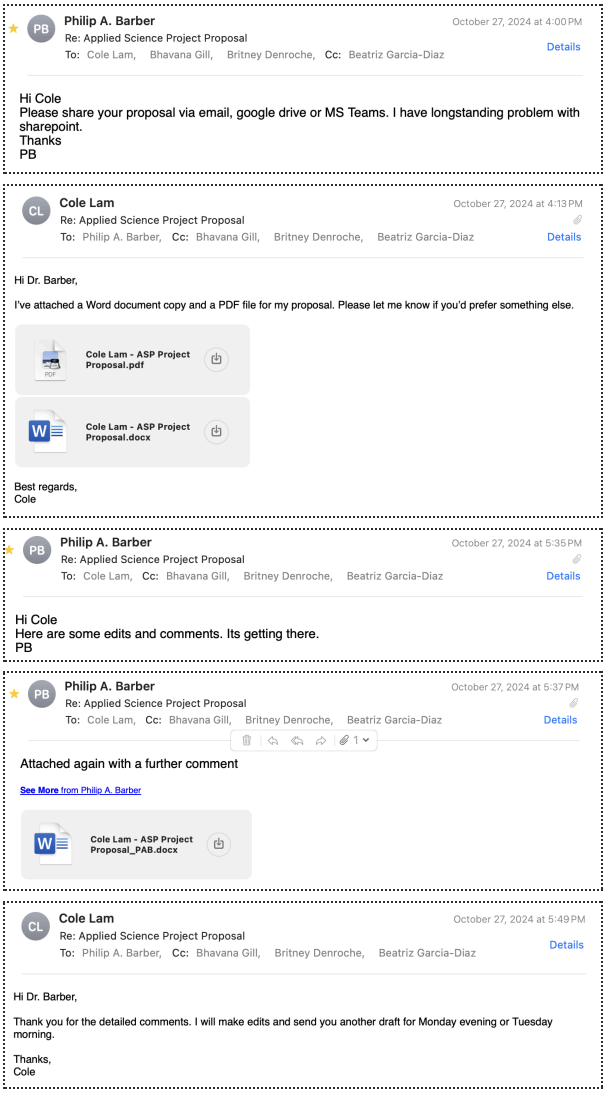
- [ ] Finish fourth draft of project proposal for Oct. 28-29 (New)
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

None

Review

This day, Dr. Barber sent some emails, firstly asking for a different way of sharing my document, and then with some edits to the proposal. I responded by saying that I would send him another draft for Monday evening or Tuesday morning so he could review the proposal again before the Wednesday meeting, if he wanted to. That evening, I began making edits to my project proposal, specifically focusing on the Background and Objectives sections (making the background section more concise, and expanding my objectives).



Philip A. Barber October 27, 2024 at 4:00 PM
Re: Applied Science Project Proposal
To: Cole Lam, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Hi Cole
Please share your proposal via email, google drive or MS Teams. I have longstanding problem with sharepoint.
Thanks
PB

Cole Lam October 27, 2024 at 4:13 PM
Re: Applied Science Project Proposal
To: Philip A. Barber, Cc: Bhavana Gill, Britney Denroche, Beatriz Garcia-Diaz Details

Hi Dr. Barber,

I've attached a Word document copy and a PDF file for my proposal. Please let me know if you'd prefer something else.

Cole Lam - ASP Project Proposal.pdf

Cole Lam - ASP Project Proposal.docx

Best regards,
Cole

Philip A. Barber October 27, 2024 at 5:35 PM
Re: Applied Science Project Proposal
To: Cole Lam, Cc: Bhavana Gill, Britney Denroche, Beatriz Garcia-Diaz Details

Hi Cole
Here are some edits and comments. Its getting there.
PB

Philip A. Barber October 27, 2024 at 5:37 PM
Re: Applied Science Project Proposal
To: Cole Lam, Cc: Bhavana Gill, Britney Denroche, Beatriz Garcia-Diaz Details

Attached again with a further comment

See More from Philip A. Barber

Cole Lam - ASP Project Proposal_PAB.docx

Cole Lam October 27, 2024 at 5:49 PM
Re: Applied Science Project Proposal
To: Philip A. Barber, Cc: Bhavana Gill, Britney Denroche, Beatriz Garcia-Diaz Details

Hi Dr. Barber,

Thank you for the detailed comments. I will make edits and send you another draft for Monday evening or Tuesday morning.

Thanks,
Cole

Notes

1. Project Proposal due October 31

October 28, 2024

Tasks To-do

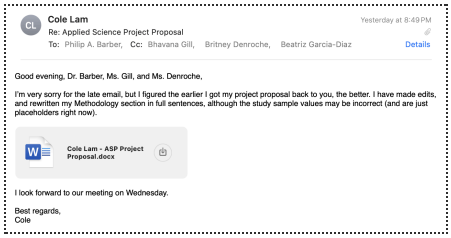
- [ ] **Project proposal due Oct. 31**
- [ ] Finish the CITI Course
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

- [x] Finish fourth draft of project proposal for Oct. 28-29

Review

This evening, I made my final edits to my project proposal, integrating all of Dr. Barber's comments, particularly asking for my Methodology to be written in sentences and not in bullet points, like he had initially said, was fine. Once that was edited, I sent the proposal back to Dr. Barber.



Cole Lam
Yesterday at 8:49 PM
Re: Applied Science Project Proposal
To: Philip A. Barber, Cc: Bhavana Gill, Britney Denroche, Beatriz Garcia-Diaz
Details

Good evening, Dr. Barber, Ms. Gill, and Ms. Denroche,

I'm very sorry for the late email, but I figured the earlier I got my project proposal back to you, the better. I have made edits, and rewritten my Methodology section in full sentences, although the study sample values may be incorrect (and are just placeholders right now).

Cole Lam - ASP Project Proposal.docx

I look forward to our meeting on Wednesday.

Best regards,
Cole

By this time, I had not finished the CITI course, despite the deadline the day before, so my new set goal was October 31, and I completed two of the modules then.

Notes

1. Project Proposal due October 31

October 29, 2024

Tasks To-do

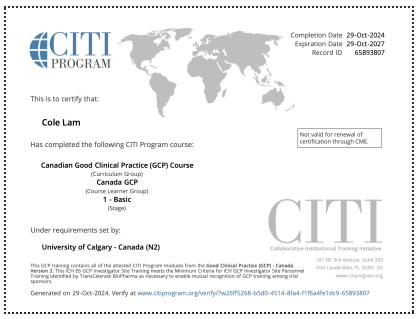
- [ ] **Project proposal due Oct. 31**
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

- [x] Finish the CITI Course

Review

This class, my focus, after properly updating my project proposal, was completing one more CITI module. My project proposal was already sent to Dr. Barber, so my time could be allocated towards the ethics courses. At the beginning of the class, Dr. Garcia talked about how to properly and efficiently use Paperpile, and also how the CYSF portal information needs to be updated promptly.
This evening, I completed the last two CITI modules to complete the CITI Canada GCP course.



CITI PROGRAM

Completion Date 29-Oct-2024
Expiration Date 29-Oct-2027
Record ID 65893807

This is to certify that:

Cole Lam

Has completed the following CITI Program course:

Not valid for renewal of certification through CME.

Canadian Good Clinical Practice (GCP) Course
(Curriculum Group)
Canada GCP
(Course Learner Group)
1 - Basic
(Stage)

Under requirements set by:

University of Calgary - Canada (N2)

CITI
Collaborative Institutional Training Initiative

111 NE 3rd Avenue, Suite 320
Fort Lauderdale, FL 33301 US
www.citiprogram.org

This GCP training contains all of the attested CITI Program modules from the Good Clinical Practice (GCP) - Canada Version 2. This ICH E6 GCP Investigator Site Training meets the Minimum Criteria for ICH GCP Investigator Site Personnel Training identified by TransCelerate BioPharma as necessary to enable mutual recognition of GCP training among trial sponsors.

Generated on 29-Oct-2024. Verify at www.citiprogram.org/verify/?w2fff5268-b5d0-4514-8fa4-f1f6a4fe1dc9-65893807

Notes

1. Project Proposal due October 31

October 30, 2024

Tasks To-do

- [ ] **Project proposal due Oct. 31**
- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

None

Review

During the lunch hour, I met with Dr. Barber to finalize edits to my project proposal. He pointed out two things to me: word choice for “cognitive decline” vs “cognition” and that I shouldn’t use “cognitive decline” when I only have one predictive measure. The other was just flow, and making sure that it would make sense for most people to read.
After that, we discussed what I would work on for November. Because they had not collected all of the data, I would work on my final paper (Introduction, Methodology), finish the remaining ethics courses, learn how to conduct some of the statistical analyses, and keep reading up on literature.
That evening, I made my edits to my proposal and uploaded it to the submission, although I did not click the “Submit” button yet.
I also started working on my oral presentation (actual powerpoint), which I created using Powerpoint. I made sure to choose a very simple design (only white) in order to make sure that the presentation is focused.

Notes

1. Project Proposal due October 31
2. Meeting with Dr. Barber at 11:30 AM

October 31, 2024

Tasks To-do

- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course

Tasks Completed

- [x] **Project proposal due Oct. 31**

Review

In class, I spent most of my time finalizing my project proposal for grammar and also making sure that my citations were correct. After that, I submitted my logbook for monthly review, and I continued working on my oral presentation. Specifically, I was working on the background section and methodology section, because those would be the hardest to describe in the short timeframe we have.

Notes

1. Project Proposal due today

Daily Notes

November 2, 2024

Tasks To-do

- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Oral Presentation For Nov. 8 (New)

Tasks Completed

None

Review

This morning, I went through the feedback that Dr. Garcia gave to me for my logbook. Specifically, it was that she wanted me to add dates to my background research section so she could cross reference both my daily notes with my research. I added that in, and also made a few formatting modifications to my Daily Notes section so that it wouldn't take up so much space.

Notes

None

November 4, 2024

Tasks To-do

- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Oral Presentation For Nov. 8 (New)

Tasks Completed

None

Review

This class, Dr. Garcia gave us work time for our oral presentations. From the previous work sessions, I had completed about half of my research and the beginning of my methods, so during the class time, I finished creating my entire Powerpoint presentation and cited all of the figures that I added (healthy brain versus demented, TIA diagram, MRI, APOE statistics, PREVENT protocol). I also started creating the bullet points for the oral component.

Notes

None

November 6, 2024

Tasks To-do

- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Oral Presentation For Nov. 8 (New)

Tasks Completed

None

Review

During this class, Eleanor and Marie-Elise presented their project proposals, but I moved to Room 303 to continue finalizing my presentation. I finished reviewing all of my powerpoint slides and bullet points for presenting, and I also presented a short excerpt to Nina, who gave some tips on making the presentation more interesting (not talking so fast). This evening, I also continued practicing my presentation, but found that my timing was really long (far over 10 minutes). So, I emailed Dr. Garcia to see whether or not the lengthier presentation would be a problem.

Notes

None

November 7, 2024

Tasks To-do

- [ ] Finish Lab Safety Course
- [ ] Finish Biosafety Program
- [ ] Finish Biosafety Bloodborne Pathogens Course
- [ ] Oral Presentation For Nov. 8 (New)

Tasks Completed

None

Notes

1. Oral Presentation tomorrow

Review

This morning, Dr. Garcia responded to my email, saying that she was willing to listen to my presentation over the lunch hour to see where timing could be cut. During this session, we found that my presentation wasn't as long as I had thought it would be (11-12 minutes vs. 16-18 minutes). Nonetheless, she still gave me a few more comments about where I could talk less, if necessary, and what ideas I could elucidate more for a higher mark. In particular, she noted that I could spend more time talking about the figures so it would be easier for people to understand. That evening, I made my final edits to my powerpoint presentation (Cole Lam - ASP Oral Presentation).

November 8, 2024

Tasks To-do	Tasks Completed	Notes
☐ Finish Lab Safety Course ☐ Finish Biosafety Program ☐ Finish Biosafety Bloodborne Pathogens Course ☐ Complete the Significant Risk Form 2B for CYSF (New)	☑ Oral Presentation For Nov. 8 (New)	None

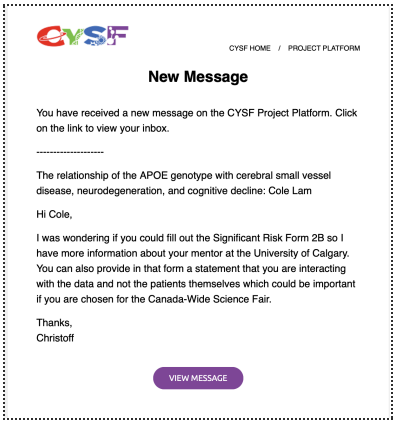
Review

During class, I presented my oral presentation, and then listened to Lauren, Coco, and Nina's presentations as well, creating the notes listed below.
Oral Presentation Notes:

- Lauren:
  - Finding a middle steps for approaching lung cancer
  - Background:
    - Lung cancer has a very high mortality rate
    - Stage 3:
      - Stage 3A vs 3B vs 3C is defined by tumor size
    - Non-small cell lung cancer (NSCLC)
    - Treatment standards:
      - Surgery
      - Radiation Therapy
      - Chemotherapy
      - Chemoradiation
      - Medication
      - Immunotherapy
      - Question: is there a reason that immunotherapy follows chemotherapy?
  - Research Question:
    - Are there interventions for treating NSCLC
  - Goals:
    - Identify potential interventions
  - Methods (systematic review):
    - Find articles
    - Exclude articles (20 year period)
    - Identify interventions that display the trends
    - Score the interventions and hypothesize the impacts
      - Will certain factors of intervention bear more significance than others?
- Coco:
  - Background:
    - Electromyography: measures electrical signals from muscle movements
      - Used for clinical assessment
      - Physical therapy
    - Muscle contractions:
      - Signal travels from the brain, to the spinal cord (motor neurons), to muscle fibers
    - Signals are amplified to better show the electrical signals in an EMG

        - Most common electrodes: planar silver wet electrodes
            - Takes a long time to prepare
            - Can be irritating
            - Reduced signal resolution
            - Motion artifact: electrodes modify the signals
        - New method: microneedle arrays (MNA)
            - Painless
            - Higher signal resolution
            - Wire-bonded MNAs:
                - This version can be mass produced and is inexpensive
    - Research question:
        - Are wire bonded MNAs more effective than current clinical practices?
    - Objectives:
        - Comparing looking at impedance (resistance for a signal to be noticed), noise amplitude, signal amplitude
        - Strengths vs weaknesses of wire-bonded MNAs
    - Methods:
        - Human skin is simulated, and then a signal generator creates a signal to be observed
    - Variables:
        - Manipulated: 3M red dot planar electrodes vs. wire-bonded MNAs
        - Response: function of the electrodes
        - Confounding: variation in skin tissue
    - Hypothesis: wire-bonded MNAs will be more effective
    - Significance: MNAs are higher quality, cheap to produce, better performance → better for clinical use
- Nina:
    - Background:
        - Psychedelics: vision distortion, used to break addictions
            - She'll be looking at classical psychedelics
            - Serotonin receptor
                - Helps regulate mood, sleep, appetite
        - Expectation vs outcome:
            - Psychedelic outcomes are highly subjective (expectations)
    - Research: how are motivations/expectations related to psilocybin-assisted therapy experiences?
    - Variables:
        - Independent variable: patient motivations and expectations
        - Dependent variable: changes in alcohol consumption
        - Controls (22-65)
    - Goals:
        - Collect data and observe trends
        - Fill in gaps of knowledge about this project
    - Significance:
        - Allows psychiatrists to tailor psilocybin treatments, which is particularly useful for psilocybin use
        - "How many drinks have they had?"
            - Question: how does this experiment plan on determining the number of drinks each participant had while minimizing response bias?
        - Question: So if your control group is given a dose of psilocybin, is your experiment planning on analyzing the impact of different dosages of psilocybin?
    - Methodology:
        - Baseline visits ask for data about their motivations/expectations, etc.
        - Weekly psychotherapy sessions

This evening, I also got an email from the CYSF, which requested that I complete the Significant Risk Form 2B, even though my ethics were already approved.



CYSF HOME / PROJECT PLATFORM

New Message

You have received a new message on the CYSF Project Platform. Click on the link to view your inbox.

The relationship of the APOE genotype with cerebral small vessel disease, neurodegeneration, and cognitive decline: Cole Lam

Hi Cole,

I was wondering if you could fill out the Significant Risk Form 2B so I have more information about your mentor at the University of Calgary. You can also provide in that form a statement that you are interacting with the data and not the patients themselves which could be important if you are chosen for the Canada-Wide Science Fair.

Thanks,
Christoff

VIEW MESSAGE

November 9, 2024

Tasks To-do

- [ ] Finish Lab Safety Course
- [ ] Complete the Significant Risk Form 2B for CYSF

Tasks Completed

- [x] Finish Biosafety Program
- [x] Finish Biosafety Bloodborne Pathogens Course
- [x] Finish WHMIS 2015 (New)

Review

This afternoon, I continued on my ethics courses, which I need to have done ASAP. I wanted to start on the Lab Safety Course, but upon attempting to register, I realized that the WHMIS 2015 course was a prerequisite that I would need to complete. I started by finishing that, and then I proceeded to complete the Biosafety Program and the Biosafety Bloodborne Pathogens Courses, which were related to each other.

Notes

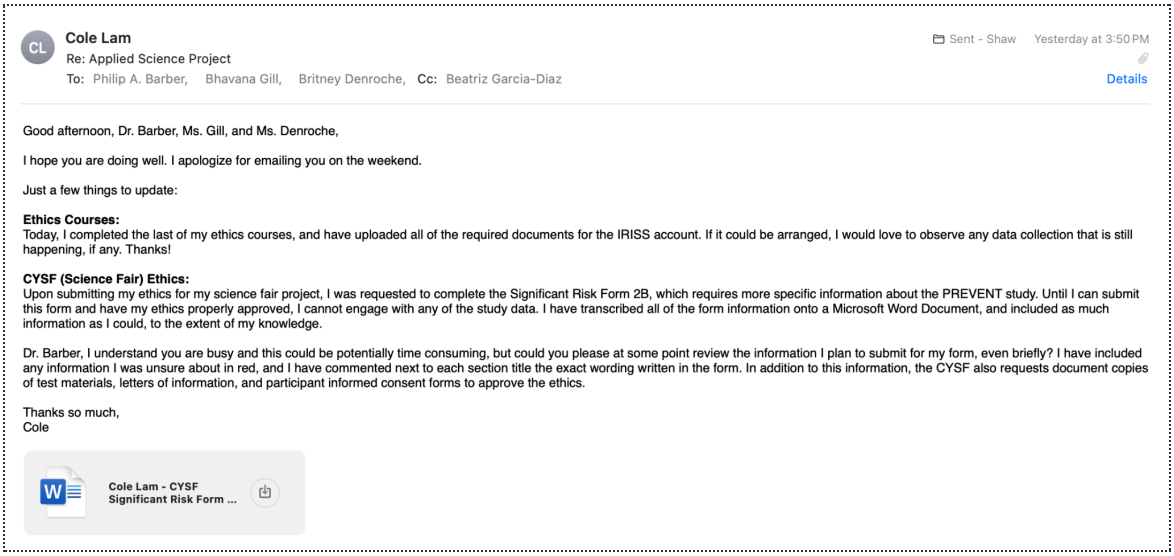
None

November 10, 2024

Tasks To-do	Tasks Completed	Notes
☐ Complete the Significant Risk Form 2B for CYSF	☑ Finish Lab Safety Course	None

Review

This afternoon, I worked to complete the Lab Safety Course. In finishing it, I had completed all of the required ethics courses for my ASP work.
Afterward, I began working on the Significant Risk Form 2B, which requires a lot of detail about the work I am doing. In particular, it asks for specific information about participant recruitment, examples of the informed consent forms, and more. I converted all the information to a Microsoft Word document in order to make it easier, and then I sent it, along with my progress update for my ethics courses, to Dr. Barber so he could help me finish the form.



Cole Lam
Re: Applied Science Project
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz

Sent - Shaw Yesterday at 3:50 PM
Details

Good afternoon, Dr. Barber, Ms. Gill, and Ms. Denroche,

I hope you are doing well. I apologize for emailing you on the weekend.

Just a few things to update:

Ethics Courses:
Today, I completed the last of my ethics courses, and have uploaded all of the required documents for the IRISS account. If it could be arranged, I would love to observe any data collection that is still happening, if any. Thanks!

CYSF (Science Fair) Ethics:
Upon submitting my ethics for my science fair project, I was requested to complete the Significant Risk Form 2B, which requires more specific information about the PREVENT study. Until I can submit this form and have my ethics properly approved, I cannot engage with any of the study data. I have transcribed all of the form information onto a Microsoft Word Document, and included as much information as I could, to the extent of my knowledge.

Dr. Barber, I understand you are busy and this could be potentially time consuming, but could you please at some point review the information I plan to submit for my form, even briefly? I have included any information I was unsure about in red, and I have commented next to each section title the exact wording written in the form. In addition to this information, the CYSF also requests document copies of test materials, letters of information, and participant informed consent forms to approve the ethics.

Thanks so much,
Cole

Cole Lam - CYSF Significant Risk Form ...

November 13, 2024

Tasks To-do	Tasks Completed	Notes
☐ Complete the Significant Risk Form 2B for CYSF	None	None

Review

First, Dr. Garcia talked to us about keeping on top of our work, and that she has not received very many emails from people, so she is not aware of what is happening with a lot of people. She also reminded us that the science fair comes up quickly, so we need to make sure that we are driving the project to make sure that things are getting done.

Oral Presentation Notes:

- Audrey:
  - Background:
    - E. coli 0157 bacteria is a large focus, and it produces a toxin.
      - Question: what is the toxin?
      - Antibiotics are detrimental to treatment
    - Bacteriophages: viruses that inject DNA into bacteria
    - Antiviral defense systems: mutations from phage attacks
    - Single-nucleotide polymorphisms: mutations from genetic drift
  - Significance:
    - HUS impacts young children
    - Phage therapy
  - Question:
    - What changes in E. coli can help improve treatment?
  - Objectives:
    - Profile anti-phage defense systems
    - Identify single-nucleotide polymorphisms
      - Uses 4 phages: why those ones?
  - Methods:
    - Bacteria was cultured in TSB
    - Mutants were created
    - 14 phage resistant bacteria isolates were determined and sent to Quebec
    - Bioinformatic analysis:
      - Using Galaxy, which analyzes the data
      - Question: How does the use of your software identify these features? What markers are indicative of bacteriophage resistance?
- Antara:
  - Background:
    - Transition to clean energy, so making electrodes more efficient is good.
    - PEMFC (proton exchange membrane fuel cells): type of fuel cell
      - Catalyst ink: one of the most important parts of making fuel cells
      - It's where the bulk of the reactions occur, so it is really important
  - Question:
    - How do the catalyst ink parameters impact the efficacy of PEMFCs?
  - Objectives:
    - Determine impact of solvent composition on ink properties
    - Help design manufacturing parameters for applying the ink
    - Make PEMFCs more common

- Hypothesis:
  - As the ratio of isopropyl alcohol to catalyst ink increases, then catalyst ink aggregates will increase, reducing resistance
- Methods:
  - Isopropyl alcohol mixtures are first created, and then other materials/mistrues required are measured
  - Then, particle size distribution, viscosity of the ink, and the pore size are measured
  - Ionomer coverage is measured
  - The electronic and ionic resistance are measured
- Significance:
  - Increasing durability
  - Increasing performance
  - Increasing cost-effectiveness
  - Main application: vehicles (particularly heavy-duty vehicles)

November 15, 2024

Tasks To-do

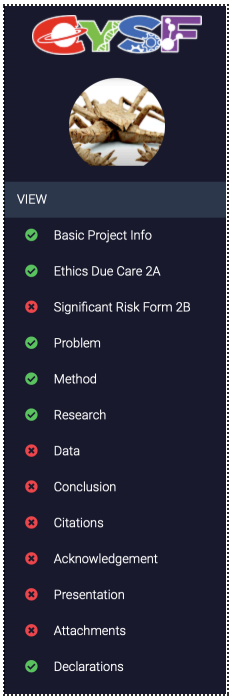
- [ ] Complete the Significant Risk Form 2B for CYSF

Tasks Completed

None

Review

During class, Dr. Garcia was away, so Mr. Rose oversaw our class. During this time, I started to fill out information for the CYSF portal. In particular, I added information into the problem, methods, and background sections, using sections from my project proposal.



Notes

None

November 19, 2024

Tasks To-do	Tasks Completed	Notes
☐ Complete the Significant Risk Form 2B for CYSF	None	None

Review

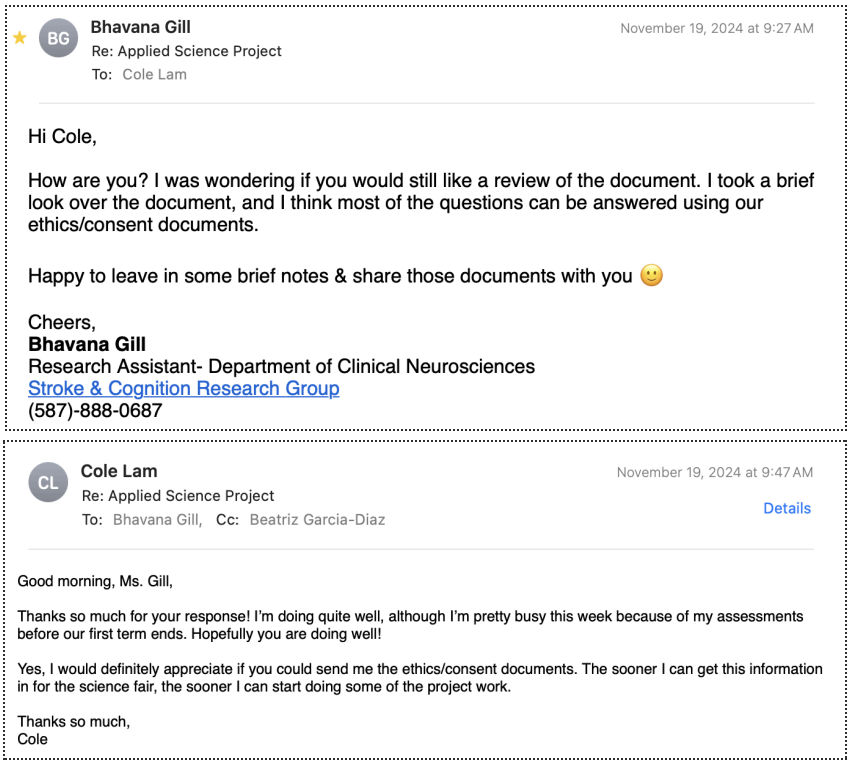
In class, I started working on my final research paper, moving elements from my project proposal to the research paper as they fit. My final research paper is written on Microsoft Word, similar to my project proposal, and I looked to add general statistics about dementia frequency in elderly populations to make the intro more broad. Then, I listened to Merrit and Maddux's project about POTS.

Oral Presentation Notes:

- Maddux/Merrit:
    - Background:
        - POTS (Postural Orthostatic Tachycardia Syndrome): abnormal heart rate and blood movement when standing
            - Why does this happen:
                - Naturally, blood flows to your legs when you are standing, so your circulatory system has baroreceptors to help mitigate this
                - But, in POTS patients, they have impaired baroreceptors
        - LBNP (Lower Body Negative Pressure): capsule for influencing blood pressure
            - Uses a vacuum and Bernoulli's principle
            - Simulates standing up by decreasing blood pressure in the legs
        - Head-Upright Tilt Test:
            - 70º to test in POTS patients
            - Used to take measurements at different angles (simulating standing)
    - Research Questions:
        - What causes POTS?
    - Hypothesis:
        - Difference is comparable between POTS patients and healthy controls
            - LBNP will simulate gravity
    - Variables:
        - Manipulated: LBNP or Tiit and LBNP or supine
        - Responding:
        - Controlled: tilt degree, physiology of patients, etc.
    - Measurements Devices:
        - Transcranial Doppler
        - Oxuneter
        - Blood Cuff
    - Measurements:
        - Heart Rate
        - Blood Pressure
        - Stroke Volume
        - Cardiac Output
        - Vascular resistance
        - Valsalva Maneuver (testing pressure)
        - Hyperventilation test
            - Used to observe blood pressure changes
        - Sinus Arrhythmia:

        - Observes blood pressure during deep breathing
- Objectives:
    - Measuring differences between LBNP and tilt test
    - Understand POTS, cardiac MRIs
- Methods:
    - Find healthy controls
    - Hooked up to devices
    - Measured measurements
    - Two groups:
        - One group gets hooked up to devices
        - One group performs valsalva maneuver, hyperventilation test, and sinus arrhythmia
- Significance:
    - Easy misdiagnosis (helps deal with this)
    - Affects a relatively large population
    - Proper simulation for cardiac MRIs

I also got an email from Bhavana, who was asking if I still needed information for my CYSF Significant Risk Form 2B, which I clarified that I did need.



Bhavana Gill November 19, 2024 at 9:27 AM
Re: Applied Science Project
To: Cole Lam

Hi Cole,

How are you? I was wondering if you would still like a review of the document. I took a brief look over the document, and I think most of the questions can be answered using our ethics/consent documents.

Happy to leave in some brief notes & share those documents with you 🙂

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam November 19, 2024 at 9:47 AM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz
Details

Good morning, Ms. Gill,

Thanks so much for your response! I'm doing quite well, although I'm pretty busy this week because of my assessments before our first term ends. Hopefully you are doing well!

Yes, I would definitely appreciate if you could send me the ethics/consent documents. The sooner I can get this information in for the science fair, the sooner I can start doing some of the project work.

Thanks so much,
Cole

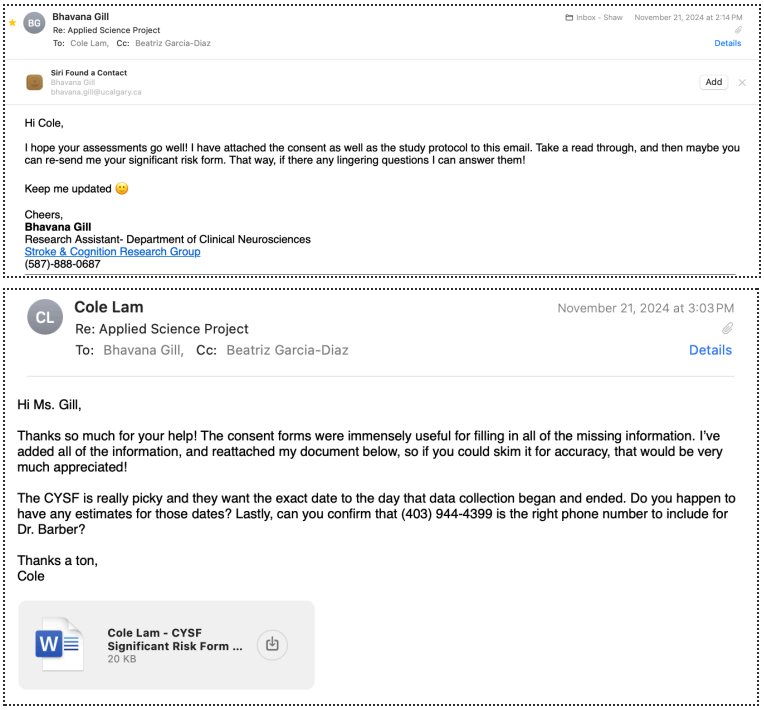
November 21, 2024

Tasks To-do	Tasks Completed	Notes
☐ Complete the Significant Risk Form 2B for CYSF	None	None

Review

This class, Dr. Garcia was participating in a safety conference, so Ms. Laidlaw oversaw our class. During this time, I continued updating my CYSF portal information, focusing on the methods section to be as specific as possible. I also wanted to write in the information in a way that showed that I did the work myself, and I wasn't just tagging along with the work of my mentor.

Bhavana also got back to me, and sent me the protocol and consent forms (PREVENT Consent Forms) that I could use to finish my form. I sent back this file (Cole Lam - Significant Risk Form 2B) to Bhavana and asked if she could briefly review it so that I can submit my ethics.



Bhavana Gill
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz
Inbox - Shaw · November 21, 2024 at 2:14 PM
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

I hope your assessments go well! I have attached the consent as well as the study protocol to this email. Take a read through, and then maybe you can re-send me your significant risk form. That way, if there any lingering questions I can answer them!

Keep me updated 🙂

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz
November 21, 2024 at 3:03 PM
Details

Hi Ms. Gill,

Thanks so much for your help! The consent forms were immensely useful for filling in all of the missing information. I've added all of the information, and reattached my document below, so if you could skim it for accuracy, that would be very much appreciated!

The CYSF is really picky and they want the exact date to the day that data collection began and ended. Do you happen to have any estimates for those dates? Lastly, can you confirm that (403) 944-4399 is the right phone number to include for Dr. Barber?

Thanks a ton,
Cole

Cole Lam - CYSF Significant Risk Form ...
20 KB

November 25, 2024

Tasks To-do	Tasks Completed	Notes
☐ Complete the Significant Risk Form 2B for CYSF	None	None

Review

In class, Dr. Garcia met with each student for ~5 minutes to discuss our progress with the project. She also mentioned to everyone some general comments. In particular, she emphasized the importance of maintaining contact with our mentors, especially during the winter holidays and midterm season, which lasts for about 3-4 weeks. I also continued with my CYSF portal information, and I also sent a follow-up email to Bhavana seeing if she could promptly review my Significant Risk Form 2B so I could submit it for ethics soon.

CL **Cole Lam** November 25, 2024 at 4:30 PM

Re: Applied Science Project

To: Bhavana Gill, Cc: Beatriz Garcia-Diaz Details

Good afternoon, Ms. Gill,

Hopefully you are doing well! I just hoped to check in and see if you have had any time to review my Significant Risk Form 2B for science fair ethics review. Last time I submitted ethics, it took them about 3 weeks to respond, so I hope to have my ethics resubmitted around Wednesday this week.

Would it be possible to have any necessary revisions for Wednesday this week? Once again, thanks so much for your help!

Thanks,
Cole

November 26, 2024

Tasks To-do	Tasks Completed	Notes
☐ Complete the Significant Risk Form 2B for CYSF	None	None

Review

Throughout today, I communicated with Bhavana, who was able to help me review my ethics form. My initial link didn't work, so I sent it again, and Bhavana was able to get feedback from Dr. Barber as well.

Bhavana Gill November 26, 2024 at 12:19 AM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

Thank you for the reminder! May you resend me the document? It won't open for some reason, but I can review it tonight and send you any edits tomorrow !

I believe Dr. Barber's office phone number is 403.944.4408- but let me ask him tomorrow morning at a meeting we have scheduled!

The data collection is ongoing, but do you need to specify an end date for the data you will be analyzing? The date our first participant was consented was 2/23/2015, but the ethics was approved on June 27, 2014. I would probably write the 2014 date 🙂!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam November 26, 2024 at 7:45 AM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz
Details

Hi Ms. Gill,

Thanks so much for your help! I've reattached the document, so hopefully this one works…

Yes, the CYSF asks for the start and end date of data collection of the study. Ultimately, I don't think it is too big of a deal if they are off by a few days or even months, but I think the CYSF just wants a general idea. You mentioned that data collection for my portion of the project may be done around mid-December, so I plan on putting that down for the end date, unless you happen to have a more specific and accurate date.

Thanks a bunch,
Cole

Cole Lam - CYSF Significant Risk Form ...
20 KB

Bhavana Gill November 26, 2024 at 2:36 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

Awesome. I think you can keep mid-December as the end date for data collection. Here is the document with some changes/comments. Dr. Barber has also reviewed 🙂! Some of the comments only show up when you click the "Comments" tab.

Let me know if you have any comments about the document.

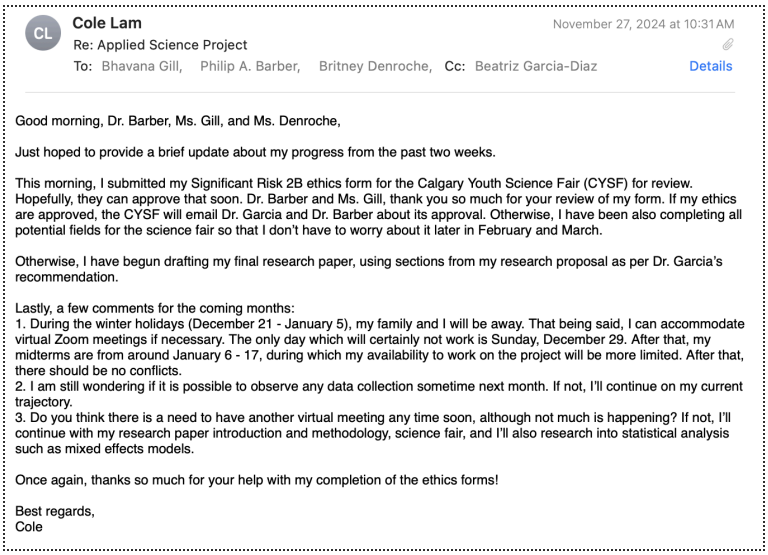
Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

November 27, 2024

Tasks To-do	Tasks Completed	Notes
None	☑ Complete the Significant Risk Form 2B for CYSF	None

Review

Today, during class, I updated all of my information for my Significant Risk 2B form, and submitted it. I then sent an email to Dr. Barber, Bhavana, and Britney updating them on my progress for science fair, as well as other things I had done this month (ie. reading, final paper, CYSF).



Cole Lam November 27, 2024 at 10:31 AM
Re: Applied Science Project
To: Bhavana Gill, Philip A. Barber, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Good morning, Dr. Barber, Ms. Gill, and Ms. Denroche,

Just hoped to provide a brief update about my progress from the past two weeks.

This morning, I submitted my Significant Risk 2B ethics form for the Calgary Youth Science Fair (CYSF) for review. Hopefully, they can approve that soon. Dr. Barber and Ms. Gill, thank you so much for your review of my form. If my ethics are approved, the CYSF will email Dr. Garcia and Dr. Barber about its approval. Otherwise, I have been also completing all potential fields for the science fair so that I don't have to worry about it later in February and March.

Otherwise, I have begun drafting my final research paper, using sections from my research proposal as per Dr. Garcia's recommendation.

Lastly, a few comments for the coming months:
1. During the winter holidays (December 21 - January 5), my family and I will be away. That being said, I can accommodate virtual Zoom meetings if necessary. The only day which will certainly not work is Sunday, December 29. After that, my midterms are from around January 6 - 17, during which my availability to work on the project will be more limited. After that, there should be no conflicts.
2. I am still wondering if it is possible to observe any data collection sometime next month. If not, I'll continue on my current trajectory.
3. Do you think there is a need to have another virtual meeting any time soon, although not much is happening? If not, I'll continue with my research paper introduction and methodology, science fair, and I'll also research into statistical analysis such as mixed effects models.

Once again, thanks so much for your help with my completion of the ethics forms!

Best regards,
Cole

November 29, 2024

Tasks To-do	Review	Notes
None	This class, Dr. Garcia was running a lab in Spanish, so we had a work block to continue with our projects. Because I didn't have any urgent work and I had other urgent work in other classes, I decided to work on Biology (Hardy-Weinberg Equilibrium Spreadsheet Assignment) in order to balance out my workload. I was still waiting for an email from Dr. Barber about moving forward, so hopefully I would get an email soon.	None

Tasks Completed
None

Daily Notes

December 5, 2024

Tasks To-do
None

Tasks Completed
None

Review
In class, Dr. Garcia talked about what is important moving forward as we move into December. First, she mentioned that our biweekly meetings are coming up, so to make sure that we are organized and staying in touch with our mentors. Then, she talked about our approaching deadlines for the sections of our final research paper. Specifically, she talked about the introduction section, which is due January 30th, and the methodology section, which is due February 19th. One really important thing that she mentioned for the methods was referencing reagents and equipment. Specifically, unlike source references, we need to reference the machinery as (model, manufacturer, location). Then, for software, we should use "Software (Version)". Lastly, the methods should be written in the present perfect (not future), because the methods have already been conducted. Then, when Dr. Garcia was meeting with other students for their biweekly meetings, I finalized updating everything I could for the CYSF portal.

Notes
None

December 9, 2024

Tasks To-do
None

Tasks Completed
None

Notes
None

Review
In class, I had a very brief biweekly meeting with Dr. Garcia. I mentioned that I wasn't doing very much right now because I was waiting for the data, so I was just working on my introduction and methodology sections of my final research paper. I also asked if I should email Dr. Barber because I had not done so for a long while, which she recommended. So, after the meeting, I drafted a short email following up on the data collection.

Cole Lam 12:38 PM
Re: Applied Science Project
To: Bhavana Gill, Philip A. Barber, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Good afternoon, Dr. Barber, Ms. Gill, and Ms. Denroche,

I hope you are doing well.

Just wanted to check in before Christmas to ask about the progress for data collection and if there is anything I can do before the winter break and midterm season. This month, I have been working on my introduction for my research paper, which is due January 30th. Is there anything else you would like me to work on for the next few weeks?

Only if you would like, I'm free to meet briefly on December 13 at 10:15 AM or December 17 at 12:30 PM to discuss any plans moving forward.

Best regards,
Cole

Then, afterward, I went back to working on my research paper introduction, lengthening it with some statistics and making it more specific and clear.

December 10, 2024

Tasks To-do	Tasks Completed	Notes
☐ Select a day to observe data collection (New)	None	None

Review

This afternoon, Bhavana responded to my email clarifying whether or not I would be observing data collection. She offered December 12, December 18, or January 7th. Unfortunately, I had test conflicts for both the December dates, but I would need to make sure that the day would work.

Bhavana Gill December 10, 2024 at 1:11 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Good Afternoon Cole,

Thank you for checking in! How is the introduction writing going? We would be happy to review any drafts you have 🙂!

We think it would be good for you to come into the lab and see how we collect our data. It may be tricky with school, as we do appointments Monday to Friday usually between 8 am and 4 pm. Would you be able to come in for any of these dates/times? If not, when is your time off from school?

- Thursday December 12th 9 am to 1 pm
- Wednesday December 18th 9:30 am to 1:30 pm
- Tuesday January 7th 9 am to 1 pm

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Regardless, I emailed Dr. Garcia to see if Webber could make an exception for me going to see data collection, because on January 7th, I would miss three classes (Physics, GH, Statistics).

Cole Lam December 10, 2024 at 5:05 PM
Re: Applied Science Project
To: Beatriz Garcia-Diaz

Hi Dr. Garcia,

Just wanted to ask you about observing data collection, because of the three times that they provided, only Tuesday, January 7th would work (not conflicting with any assessments). This is a Day 4, meaning I will be missing Physics, GH, and most of Statistics. Is this something that Webber could arrange, or should I ask them if they have other availability?

Thanks,
Cole

Beatriz Garcia-Diaz December 10, 2024 at 6:39 PM
Re: Applied Science Project
To: Cole Lam

Cole,

Given than Jan 7th is the second day back to school from winter break and most classes are going to be reviewing for midterms, I'd say it's safe to assume you could get the teachers to allow you to miss their classes for this important and difficult-to-rescheduled opportunity to see data collection done in the lab. I will help you reach out to those teachers and make sure they understand this is an exception and won't happen very often. Also any other missed assessment or homework can be done in ASP.

Let's chat more about this tomorrow in class.

Cheers,

Dr. Garcia

December 11, 2024

Tasks To-do	Tasks Completed	Notes
☐ Select a day to observe data collection	None	None

Review

This day, I sent a brief email to Bhavana clarifying that I hope to observe data collection on January 7, but mentioned that because I would need to get an exception from Webber administration, I could not yet confirm that I could go.

Cole Lam 12:38 PM
Re: Applied Science Project
To: Bhavana Gill, Philip A. Barber, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Good afternoon, Dr. Barber, Ms. Gill, and Ms. Denroche,

I hope you are doing well.

Just wanted to check in before Christmas to ask about the progress for data collection and if there is anything I can do before the winter break and midterm season. This month, I have been working on my introduction for my research paper, which is due January 30th. Is there anything else you would like me to work on for the next few weeks?

Only if you would like, I'm free to meet briefly on December 13 at 10:15 AM or December 17 at 12:30 PM to discuss any plans moving forward.

Best regards,
Cole

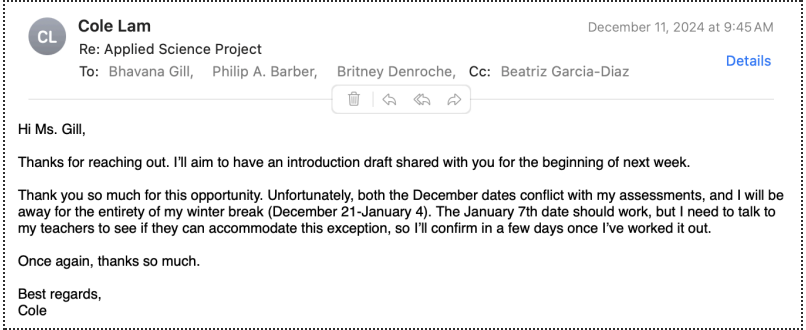
During class, I also continued working on my introduction for the research paper, making edits and restructuring the order of the information.

December 13, 2024

Tasks To-do	Tasks Completed	Notes
None	☑ Select a day to observe data collection	None

Review

This morning, I sent an email to Dr. Barber, Bhavana, and Britney telling them that I worked it out with administration and that I would be able to observe data collection on January 7th.



Cole Lam December 11, 2024 at 9:45 AM
Re: Applied Science Project
To: Bhavana Gill, Philip A. Barber, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Hi Ms. Gill,

Thanks for reaching out. I'll aim to have an introduction draft shared with you for the beginning of next week.

Thank you so much for this opportunity. Unfortunately, both the December dates conflict with my assessments, and I will be away for the entirety of my winter break (December 21-January 4). The January 7th date should work, but I need to talk to my teachers to see if they can accommodate this exception, so I'll confirm in a few days once I've worked it out.

Once again, thanks so much.

Best regards,
Cole

I had also finalized my first draft for my introduction for the final research paper, and asked Dr. Garcia to review it. I sent her the document so that I could make her edits and send Dr. Barber the draft at the beginning of next week.

December 15, 2024

Tasks To-do	Review	Notes
None	This afternoon, I sent Starbucks digital gift certificates to Dr. Barber, Bhavana, and Britney, wishing them a merry Christmas and thanking them for their support with my Applied Science Project.	None

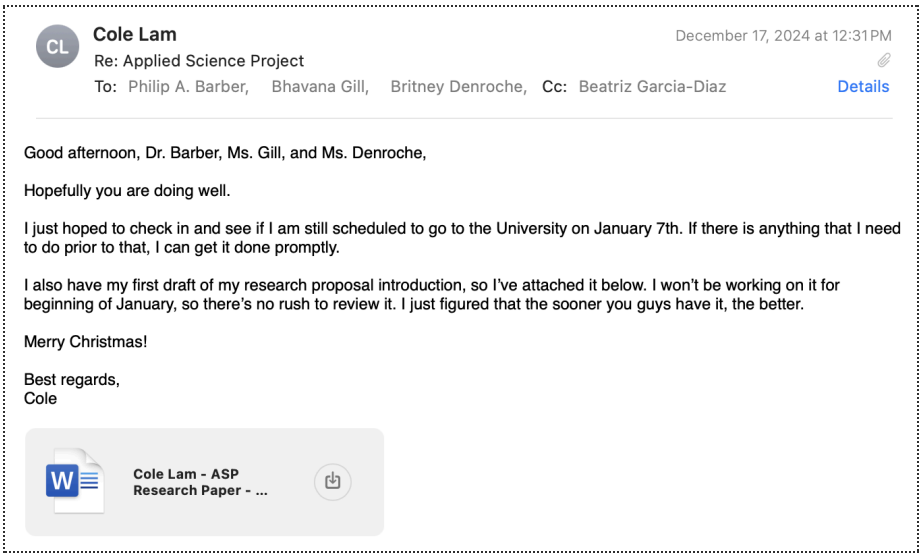
Tasks Completed
None

December 17, 2024

Tasks To-do	Tasks Completed	Notes
None	None	None

Review

During class, Dr. Garcia gave me back her recommended edits for my introduction. These included making sure I had my DOIs in my citations, and then also reducing redundant wording and phrasing. Additionally, having not gotten a response in four days, I sent a follow-up email to Dr. Barber to confirm that they were able to accommodate me visiting their data collection. I also sent them my first draft of my introduction for my research paper, mentioning that I wouldn't be able to work on it for a while because of midterm season.



Cole Lam December 17, 2024 at 12:31 PM
Re: Applied Science Project
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

Good afternoon, Dr. Barber, Ms. Gill, and Ms. Denroche,

Hopefully you are doing well.

I just hoped to check in and see if I am still scheduled to go to the University on January 7th. If there is anything that I need to do prior to that, I can get it done promptly.

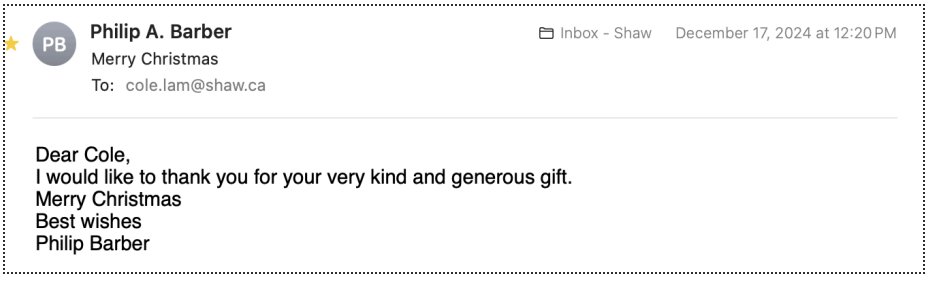
I also have my first draft of my research proposal introduction, so I've attached it below. I won't be working on it for beginning of January, so there's no rush to review it. I just figured that the sooner you guys have it, the better.

Merry Christmas!

Best regards,
Cole

Cole Lam - ASP Research Paper - ...

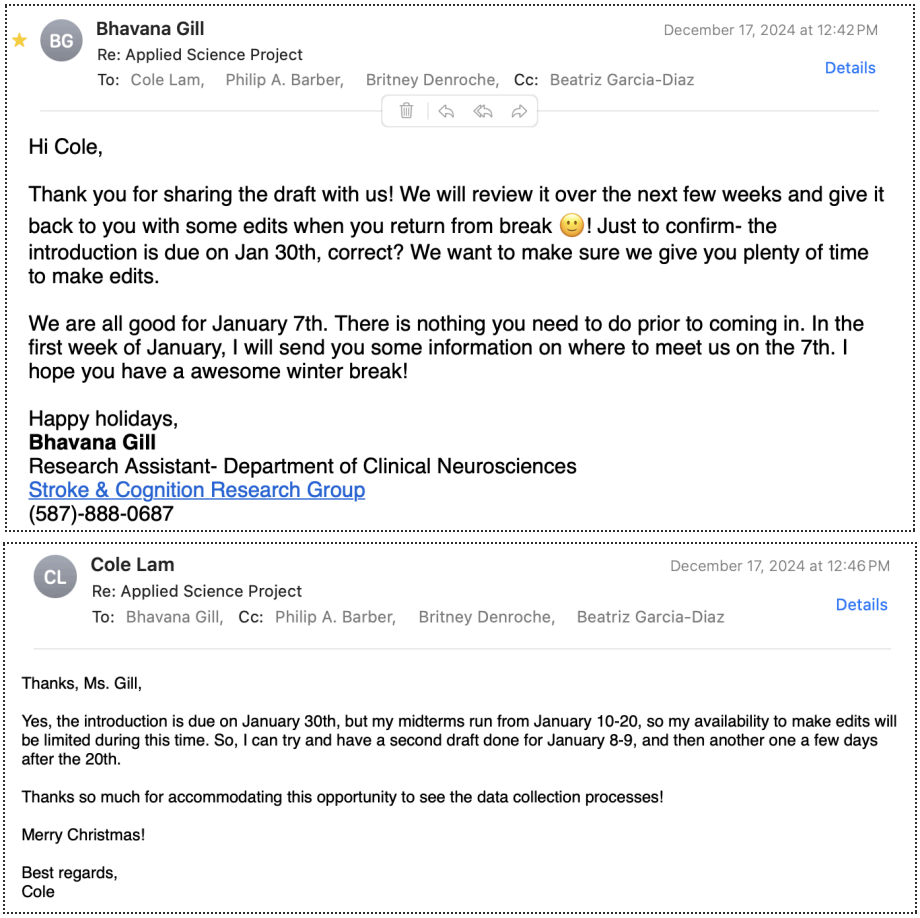
Dr. Barber also sent a thank-you email for the Starbucks gift card.



Philip A. Barber Inbox - Shaw December 17, 2024 at 12:20 PM
Merry Christmas
To: cole.lam@shaw.ca

Dear Cole,
I would like to thank you for your very kind and generous gift.
Merry Christmas
Best wishes
Philip Barber

Shortly after I sent my email to Dr. Barber and his assistants, Bhavana responded to me, saying that I would, indeed, be able to observe data collection and that there wouldn't be anything I need to do prior to it. She also wanted to confirm that my introduction for the research paper introduction is January 30th. I then responded confirming the due date, and also reminding them that midterm season would limit my availability to work on my introduction for about a week and a half.



Bhavana Gill December 17, 2024 at 12:42 PM
Re: Applied Science Project
To: Cole Lam, Philip A. Barber, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Hi Cole,

Thank you for sharing the draft with us! We will review it over the next few weeks and give it back to you with some edits when you return from break 🙂! Just to confirm- the introduction is due on Jan 30th, correct? We want to make sure we give you plenty of time to make edits.

We are all good for January 7th. There is nothing you need to do prior to coming in. In the first week of January, I will send you some information on where to meet us on the 7th. I hope you have a awesome winter break!

Happy holidays,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam December 17, 2024 at 12:46 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Philip A. Barber, Britney Denroche, Beatriz Garcia-Diaz
Details

Thanks, Ms. Gill,

Yes, the introduction is due on January 30th, but my midterms run from January 10-20, so my availability to make edits will be limited during this time. So, I can try and have a second draft done for January 8-9, and then another one a few days after the 20th.

Thanks so much for accommodating this opportunity to see the data collection processes!

Merry Christmas!

Best regards,
Cole

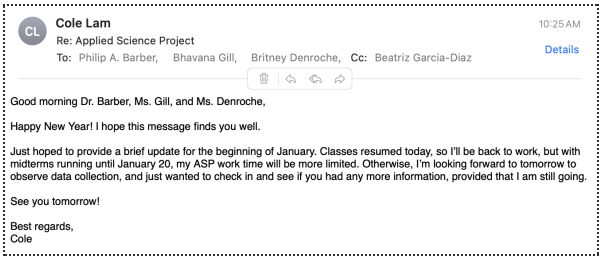
Daily Notes

January 6, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 (New)	None	1. ~~Data collection observation is at the University of Calgary tomorrow~~

Review

During class, I sent an email to Dr. Barber and his assistants just providing a brief update on the start to the new year, mentioning that classes have resumed, although my midterms are now, meaning my time to work on ASP is reduced. This morning, I still had not received an email from them about where to meet tomorrow and any other information, so I also asked about that in the email.



Cole Lam 10:25 AM
Re: Applied Science Project
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Good morning Dr. Barber, Ms. Gill, and Ms. Denroche,

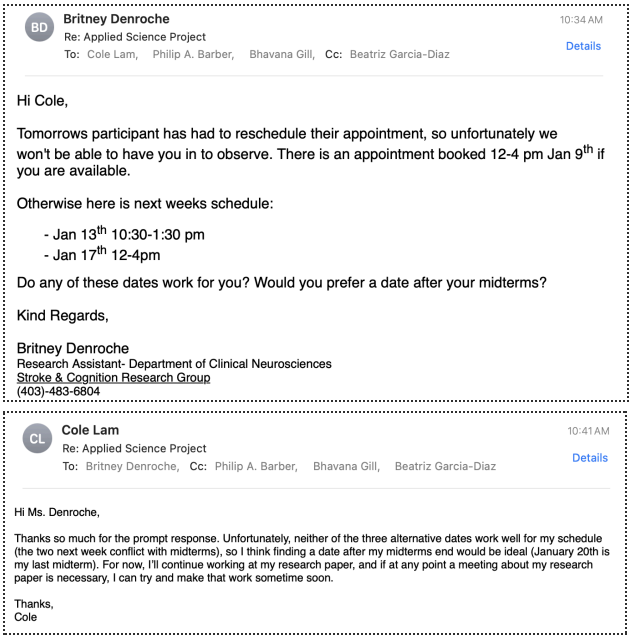
Happy New Year! I hope this message finds you well.

Just hoped to provide a brief update for the beginning of January. Classes resumed today, so I'll be back to work, but with midterms running until January 20, my ASP work time will be more limited. Otherwise, I'm looking forward to tomorrow to observe data collection, and just wanted to check in and see if you had any more information, provided that I am still going.

See you tomorrow!

Best regards,
Cole

Just a little while later, Britney responded, unfortunately reporting that the patient had to reschedule, meaning that I would need to find another time to go into the University. She provided three alternate dates, but none of them were ideal, so I responded recommending that we find a date for after midterms are done.



Britney Denroche 10:34 AM
Re: Applied Science Project
To: Cole Lam, Philip A. Barber, Bhavana Gill, Cc: Beatriz Garcia-Diaz
Details

Hi Cole,

Tomorrows participant has had to reschedule their appointment, so unfortunately we won't be able to have you in to observe. There is an appointment booked 12-4 pm Jan 9th if you are available.

Otherwise here is next weeks schedule:

- Jan 13th 10:30-1:30 pm
- Jan 17th 12-4pm

Do any of these dates work for you? Would you prefer a date after your midterms?

Kind Regards,

Britney Denroche
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(403)-483-6804

Cole Lam 10:41 AM
Re: Applied Science Project
To: Britney Denroche, Cc: Philip A. Barber, Bhavana Gill, Beatriz Garcia-Diaz
Details

Hi Ms. Denroche,

Thanks so much for the prompt response. Unfortunately, neither of the three alternative dates work well for my schedule (the two next week conflict with midterms), so I think finding a date after my midterms end would be ideal (January 20th is my last midterm). For now, I'll continue working at my research paper, and if at any point a meeting about my research paper is necessary, I can try and make that work sometime soon.

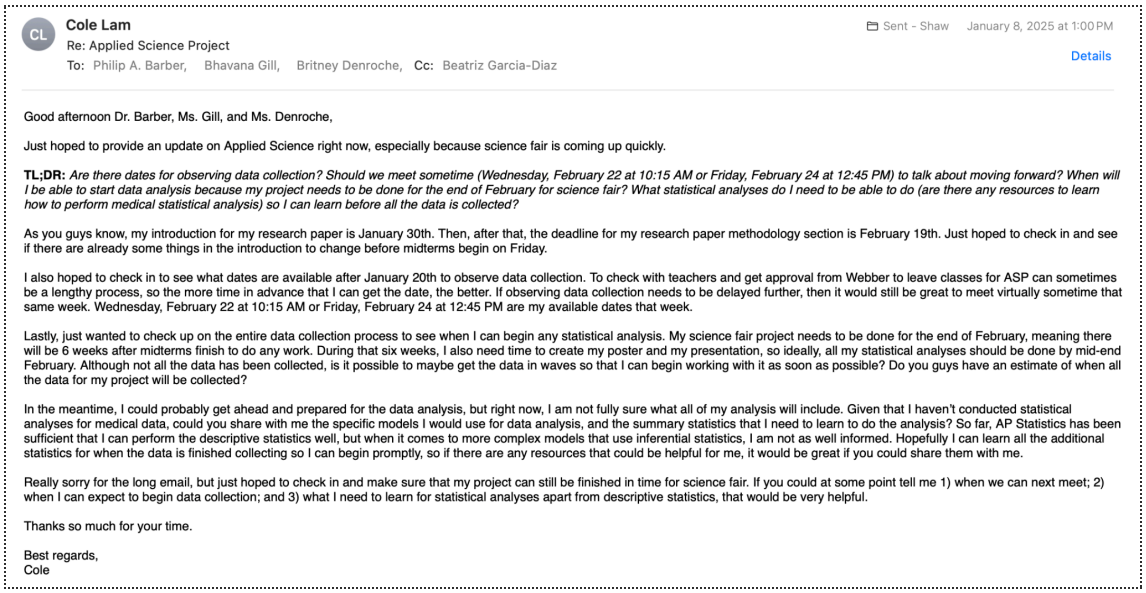
Thanks,
Cole

January 8, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30	None	None

Review

Considering that midterms were beginning in just two days, I realized that the time that I had to finish the project and prepare it for the science fair was quickly decreasing. In order to become more organized and make sure that I could have everything done, I sent a somewhat lengthy email to Dr. Barber and his assistants, asking them when the data would be in, along with all of my deadlines.



Cole Lam — Sent - Shaw — January 8, 2025 at 1:00 PM

Re: Applied Science Project

To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz

Details

Good afternoon Dr. Barber, Ms. Gill, and Ms. Denroche,

Just hoped to provide an update on Applied Science right now, especially because science fair is coming up quickly.

TL;DR: *Are there dates for observing data collection? Should we meet sometime (Wednesday, February 22 at 10:15 AM or Friday, February 24 at 12:45 PM) to talk about moving forward? When will I be able to start data analysis because my project needs to be done for the end of February for science fair? What statistical analyses do I need to be able to do (are there any resources to learn how to perform medical statistical analysis) so I can learn before all the data is collected?*

As you guys know, my introduction for my research paper is January 30th. Then, after that, the deadline for my research paper methodology section is February 19th. Just hoped to check in and see if there are already some things in the introduction to change before midterms begin on Friday.

I also hoped to check in to see what dates are available after January 20th to observe data collection. To check with teachers and get approval from Webber to leave classes for ASP can sometimes be a lengthy process, so the more time in advance that I can get the date, the better. If observing data collection needs to be delayed further, then it would still be great to meet virtually sometime that same week. Wednesday, February 22 at 10:15 AM or Friday, February 24 at 12:45 PM are my available dates that week.

Lastly, just wanted to check up on the entire data collection process to see when I can begin any statistical analysis. My science fair project needs to be done for the end of February, meaning there will be 6 weeks after midterms finish to do any work. During that six weeks, I also need time to create my poster and my presentation, so ideally, all my statistical analyses should be done by mid-end February. Although not all the data has been collected, is it possible to maybe get the data in waves so that I can begin working with it as soon as possible? Do you guys have an estimate of when all the data for my project will be collected?

In the meantime, I could probably get ahead and prepared for the data analysis, but right now, I am not fully sure what all of my analysis will include. Given that I haven't conducted statistical analyses for medical data, could you share with me the specific models I would use for data analysis, and the summary statistics that I need to learn to do the analysis? So far, AP Statistics has been sufficient that I can perform the descriptive statistics well, but when it comes to more complex models that use inferential statistics, I am not as well informed. Hopefully I can learn all the additional statistics for when the data is finished collecting so I can begin promptly, so if there are any resources that could be helpful for me, it would be great if you could share them with me.

Really sorry for the long email, but just hoped to check in and make sure that my project can still be finished in time for science fair. If you could at some point tell me 1) when we can next meet; 2) when I can expect to begin data collection; and 3) what I need to learn for statistical analyses apart from descriptive statistics, that would be very helpful.

Thanks so much for your time.

Best regards,
Cole

In class, Dr. Garcia also gave a comprehensive overview of the timeline for the next few months, stressing the importance of planning and making sure that we were on top of our projects. She also talked briefly about the science fair, mentioning that the school science fair is on March 11th, and that we would want to practice our oral presentations and have everything ready for then.

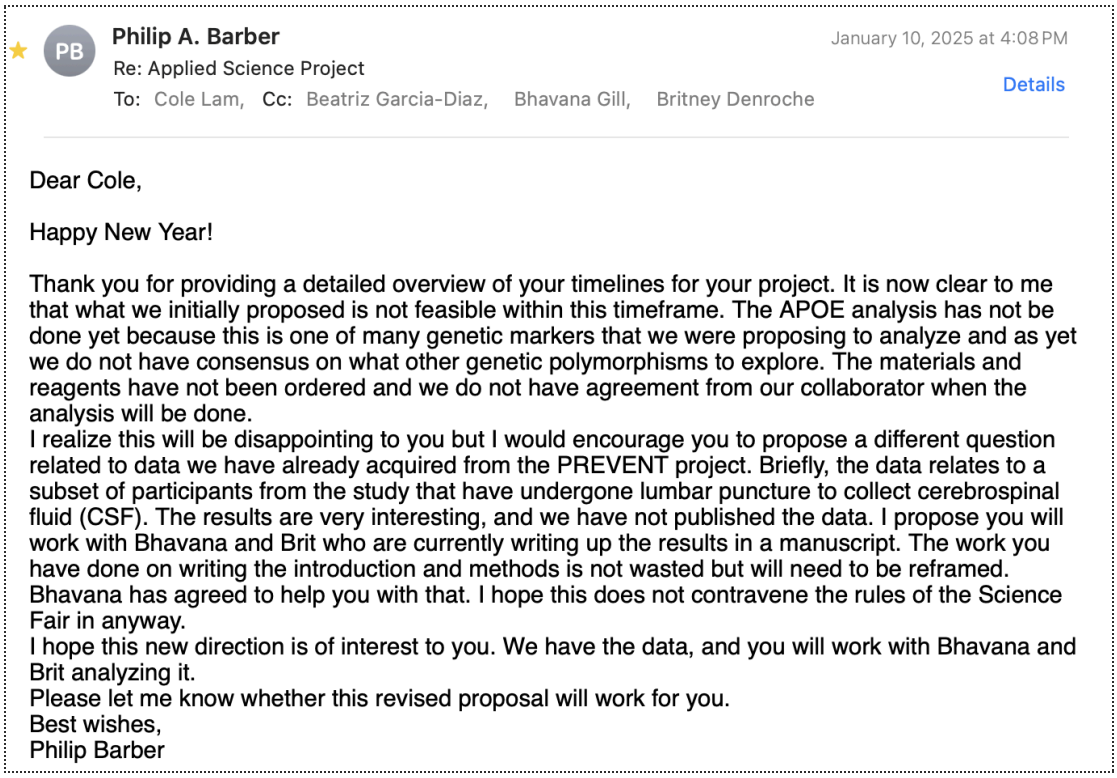
Lastly, I also asked Dr. Garcia about the current state of my project, given that I still haven't received any data, and also don't have a good idea of what kind of data analysis I will be conducting. She recommended to me that I email them again, which I had already done, and mention that tight timeline, also suggesting that if they couldn't get the data in for science fair that I pivot my project slightly to work with the data that they did have at the time.

January 10, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30	None	1. Project change!

Review

As midterms had begun, I was no longer in classes and did not complete any Applied Science Project work. However, Dr. Barber replied to my lengthy email from two days prior, mentioning that unfortunately, I would need to switch my project in order to complete it within the timeframe required for the science fair. Specifically, he mentioned that the currently collected data regards cerebrospinal fluid from lumbar punctures, and that I could hopefully adapt to that project to submit for the science fair.



Philip A. Barber January 10, 2025 at 4:08 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz, Bhavana Gill, Britney Denroche Details

Dear Cole,

Happy New Year!

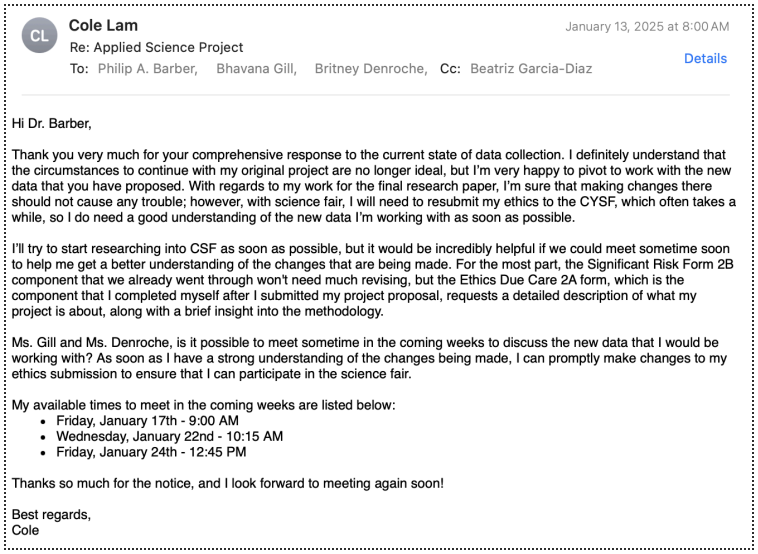
Thank you for providing a detailed overview of your timelines for your project. It is now clear to me that what we initially proposed is not feasible within this timeframe. The APOE analysis has not be done yet because this is one of many genetic markers that we were proposing to analyze and as yet we do not have consensus on what other genetic polymorphisms to explore. The materials and reagents have not been ordered and we do not have agreement from our collaborator when the analysis will be done.
I realize this will be disappointing to you but I would encourage you to propose a different question related to data we have already acquired from the PREVENT project. Briefly, the data relates to a subset of participants from the study that have undergone lumbar puncture to collect cerebrospinal fluid (CSF). The results are very interesting, and we have not published the data. I propose you will work with Bhavana and Brit who are currently writing up the results in a manuscript. The work you have done on writing the introduction and methods is not wasted but will need to be reframed. Bhavana has agreed to help you with that. I hope this does not contravene the rules of the Science Fair in anyway.
I hope this new direction is of interest to you. We have the data, and you will work with Bhavana and Brit analyzing it.
Please let me know whether this revised proposal will work for you.
Best wishes,
Philip Barber

January 13, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 ☐ Resubmit Ethics 2A and 2B (New)	None	None

Review

As to not email them on the weekend, I sent my response to Dr. Barber on the following Monday, mentioning my flexibility in pivoting projects. I did mention that it would be important to meet sometime soon, and that I may need to resubmit ethics for the science fair to work with the new data. Dr. Garcia also sent an email confirming that she could accommodate me switching projects for the science fair.



Cole Lam January 13, 2025 at 8:00 AM
Re: Applied Science Project
To: Philip A. Barber, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Hi Dr. Barber,

Thank you very much for your comprehensive response to the current state of data collection. I definitely understand that the circumstances to continue with my original project are no longer ideal, but I'm very happy to pivot to work with the new data that you have proposed. With regards to my work for the final research paper, I'm sure that making changes there should not cause any trouble; however, with science fair, I will need to resubmit my ethics to the CYSF, which often takes a while, so I do need a good understanding of the new data I'm working with as soon as possible.

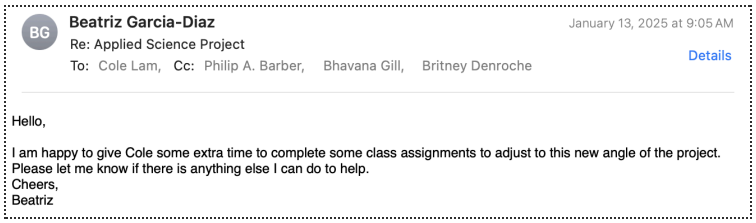
I'll try to start researching into CSF as soon as possible, but it would be incredibly helpful if we could meet sometime soon to help me get a better understanding of the changes that are being made. For the most part, the Significant Risk Form 2B component that we already went through won't need much revising, but the Ethics Due Care 2A form, which is the component that I completed myself after I submitted my project proposal, requests a detailed description of what my project is about, along with a brief insight into the methodology.

Ms. Gill and Ms. Denroche, is it possible to meet sometime in the coming weeks to discuss the new data that I would be working with? As soon as I have a strong understanding of the changes being made, I can promptly make changes to my ethics submission to ensure that I can participate in the science fair.

My available times to meet in the coming weeks are listed below:
- Friday, January 17th - 9:00 AM
- Wednesday, January 22nd - 10:15 AM
- Friday, January 24th - 12:45 PM

Thanks so much for the notice, and I look forward to meeting again soon!

Best regards,
Cole

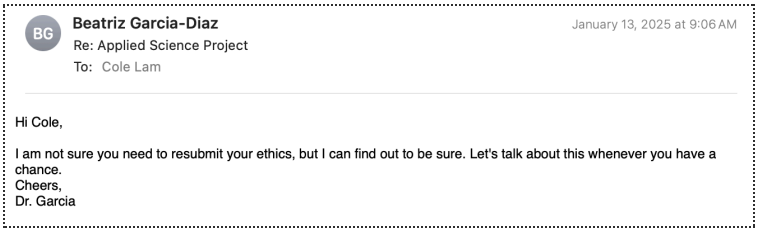


Beatriz Garcia-Diaz January 13, 2025 at 9:05 AM
Re: Applied Science Project
To: Cole Lam, Cc: Philip A. Barber, Bhavana Gill, Britney Denroche
Details

Hello,

I am happy to give Cole some extra time to complete some class assignments to adjust to this new angle of the project. Please let me know if there is anything else I can do to help.
Cheers,
Beatriz

She also sent an email to me, mentioning that there may not be a need to resubmit my ethics, but she was going to check with the CYSF ethics committee to confirm this.



Beatriz Garcia-Diaz January 13, 2025 at 9:06 AM
Re: Applied Science Project
To: Cole Lam

Hi Cole,

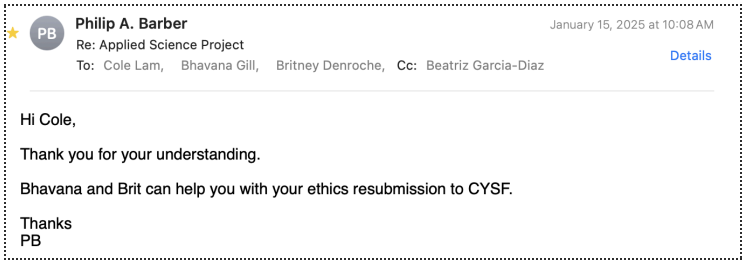
I am not sure you need to resubmit your ethics, but I can find out to be sure. Let's talk about this whenever you have a chance.
Cheers,
Dr. Garcia

January 15, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 ☐ ~~Resubmit Ethics 2A and 2B~~	None	None

Review

Dr. Barber sent a brief response that day, mentioning that Bhavana and Britney could help me review my ethics.



PB **Philip A. Barber** January 15, 2025 at 10:08 AM
Re: Applied Science Project
To: Cole Lam, Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz Details

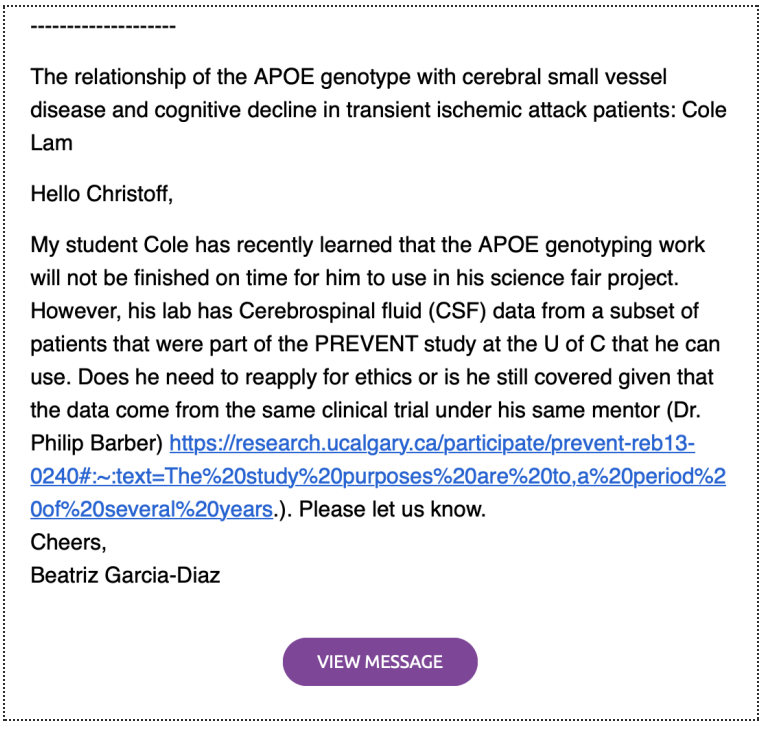
Hi Cole,

Thank you for your understanding.

Bhavana and Brit can help you with your ethics resubmission to CYSF.

Thanks
PB

Additionally, Dr. Garcia sent a message to the CYSF, as I was busy during midterms, clarifying if I would need to resubmit my ethics. A member of the ethics committee confirmed that I would not need to resubmit my ethics, and also approved my Significant Risk 2B form.



The relationship of the APOE genotype with cerebral small vessel disease and cognitive decline in transient ischemic attack patients: Cole Lam

Hello Christoff,

My student Cole has recently learned that the APOE genotyping work will not be finished on time for him to use in his science fair project. However, his lab has Cerebrospinal fluid (CSF) data from a subset of patients that were part of the PREVENT study at the U of C that he can use. Does he need to reapply for ethics or is he still covered given that the data come from the same clinical trial under his same mentor (Dr. Philip Barber) https://research.ucalgary.ca/participate/prevent-reb13-0240#:~:text=The%20study%20purposes%20are%20to,a%20period%20of%20several%20years.). Please let us know.
Cheers,
Beatriz Garcia-Diaz

VIEW MESSAGE

CYSF HOME / PROJECT PLATFORM

New Message

You have received a new message on the CYSF Project Platform. Click on the link to view your inbox.

The relationship of the APOE genotype with cerebral small vessel disease and cognitive decline in transient ischemic attack patients: Cole Lam

Significant Risk Form 2B for project 'The relationship of the APOE genotype with cerebral small vessel disease and cognitive decline in transient ischemic attack patients: Cole Lam' is approved.

VIEW MESSAGE

CYSF HOME / PROJECT PLATFORM

New Message

You have received a new message on the CYSF Project Platform. Click on the link to view your inbox.

The relationship of the APOE genotype with cerebral small vessel disease and cognitive decline in transient ischemic attack patients: Cole Lam

Hi Beatriz,

Thank you very much for letting me know. The student does not need to reapply for ethics as long as they are still only interacting with participants' data and not directly with the patients.

Have a great rest of your week!
Christoff

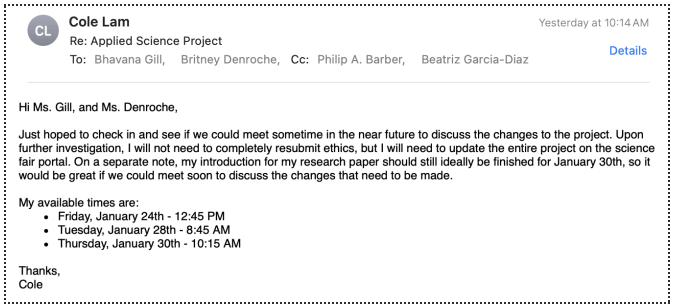
VIEW MESSAGE

January 22, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30	None	None

Review

With midterms finishing, and still not having heard from Dr. Barber about a potential meeting time to discuss the project changes, I sent a follow-up email seeing if I could meet with his assistants sometime that week.



Cole Lam — Yesterday at 10:14 AM
Re: Applied Science Project
To: Bhavana Gill, Britney Denroche, Cc: Philip A. Barber, Beatriz Garcia-Diaz
Details

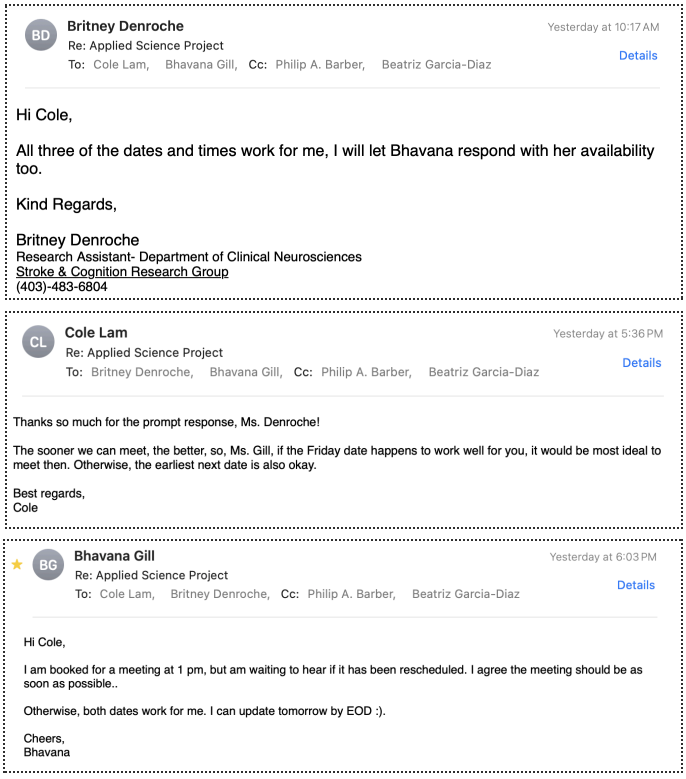
Hi Ms. Gill, and Ms. Denroche,

Just hoped to check in and see if we could meet sometime in the near future to discuss the changes to the project. Upon further investigation, I will not need to completely resubmit ethics, but I will need to update the entire project on the science fair portal. On a separate note, my introduction for my research paper should still ideally be finished for January 30th, so it would be great if we could meet soon to discuss the changes that need to be made.

My available times are:
- Friday, January 24th - 12:45 PM
- Tuesday, January 28th - 8:45 AM
- Thursday, January 30th - 10:15 AM

Thanks,
Cole

Britney responded, confirming all times were able to work, so I sent another email acknowledging that, also mentioning that this Friday would be the most ideal date so I could get the best understanding of the changes as soon as possible. Bhavana then mentioned that the latter two dates would work, and that she may be able to meet on Friday if she can move a meeting.



Britney Denroche — Yesterday at 10:17 AM
Re: Applied Science Project
To: Cole Lam, Bhavana Gill, Cc: Philip A. Barber, Beatriz Garcia-Diaz
Details

Hi Cole,

All three of the dates and times work for me, I will let Bhavana respond with her availability too.

Kind Regards,

Britney Denroche
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(403)-483-6804

Cole Lam — Yesterday at 5:36 PM
Re: Applied Science Project
To: Britney Denroche, Bhavana Gill, Cc: Philip A. Barber, Beatriz Garcia-Diaz
Details

Thanks so much for the prompt response, Ms. Denroche!

The sooner we can meet, the better, so, Ms. Gill, if the Friday date happens to work well for you, it would be most ideal to meet then. Otherwise, the earliest next date is also okay.

Best regards,
Cole

Bhavana Gill — Yesterday at 6:03 PM
Re: Applied Science Project
To: Cole Lam, Britney Denroche, Cc: Philip A. Barber, Beatriz Garcia-Diaz
Details

Hi Cole,

I am booked for a meeting at 1 pm, but am waiting to hear if it has been rescheduled. I agree the meeting should be as soon as possible..

Otherwise, both dates work for me. I can update tomorrow by EOD :).

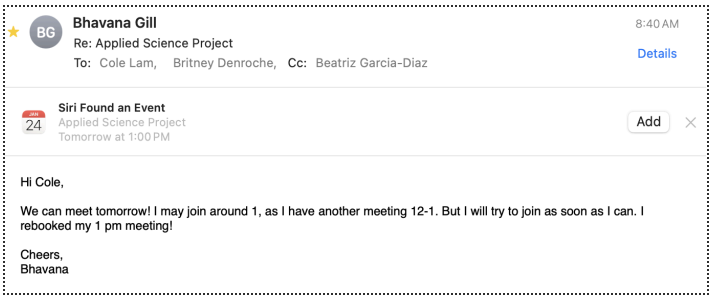
Cheers,
Bhavana

January 23, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30	None	1. Meeting with Bhavana and Britney tomorrow at 1:00 PM

Review

This morning, Bhavana confirmed that she could meet on Friday, although that she had a different meeting from 12-1 PM, so she would have to come fifteen minutes later. I mentioned that I had flexibility with my class, so meeting fifteen minutes later would cause no problems.



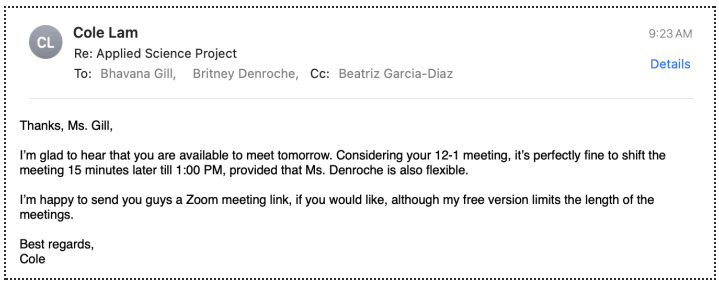
Bhavana Gill 8:40 AM
Re: Applied Science Project
To: Cole Lam, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Siri Found an Event
Applied Science Project
Tomorrow at 1:00 PM
Add

Hi Cole,

We can meet tomorrow! I may join around 1, as I have another meeting 12-1. But I will try to join as soon as I can. I rebooked my 1 pm meeting!

Cheers,
Bhavana



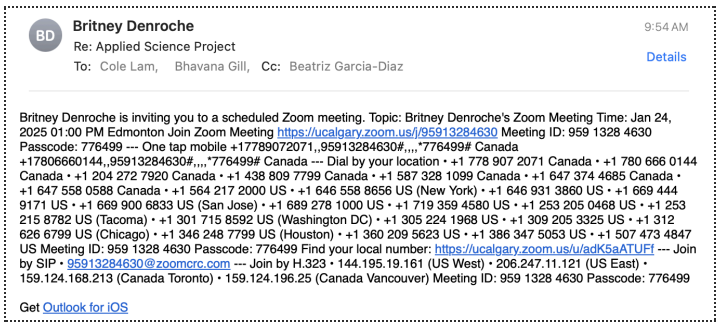
Cole Lam 9:23 AM
Re: Applied Science Project
To: Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz
Details

Thanks, Ms. Gill,

I'm glad to hear that you are available to meet tomorrow. Considering your 12-1 meeting, it's perfectly fine to shift the meeting 15 minutes later till 1:00 PM, provided that Ms. Denroche is also flexible.

I'm happy to send you guys a Zoom meeting link, if you would like, although my free version limits the length of the meetings.

Best regards,
Cole



Britney Denroche 9:54 AM
Re: Applied Science Project
To: Cole Lam, Bhavana Gill, Cc: Beatriz Garcia-Diaz
Details

Britney Denroche is inviting you to a scheduled Zoom meeting. Topic: Britney Denroche's Zoom Meeting Time: Jan 24, 2025 01:00 PM Edmonton Join Zoom Meeting https://ucalgary.zoom.us/j/95913284630 Meeting ID: 959 1328 4630 Passcode: 776499 --- One tap mobile +17789072071,,95913284630#,,,,*776499# Canada +17806660144,,95913284630#,,,,*776499# Canada --- Dial by your location • +1 778 907 2071 Canada • +1 780 666 0144 Canada • +1 204 272 7920 Canada • +1 438 809 7799 Canada • +1 587 328 1099 Canada • +1 647 374 4685 Canada • +1 647 558 0588 Canada • +1 564 217 2000 US • +1 646 558 8656 US (New York) • +1 646 931 3860 US • +1 669 444 9171 US • +1 669 900 6833 US (San Jose) • +1 689 278 1000 US • +1 719 359 4580 US • +1 253 205 0468 US • +1 253 215 8782 US (Tacoma) • +1 301 715 8592 US (Washington DC) • +1 305 224 1968 US • +1 309 205 3325 US • +1 312 626 6799 US (Chicago) • +1 346 248 7799 US (Houston) • +1 360 209 5623 US • +1 386 347 5053 US • +1 507 473 4847 US Meeting ID: 959 1328 4630 Passcode: 776499 Find your local number: https://ucalgary.zoom.us/u/adK5aATUFf --- Join by SIP • 95913284630@zoomcrc.com --- Join by H.323 • 144.195.19.161 (US West) • 206.247.11.121 (US East) • 159.124.168.213 (Canada Toronto) • 159.124.196.25 (Canada Vancouver) Meeting ID: 959 1328 4630 Passcode: 776499

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Over the lunch hour, our science fair coordinators held a meeting, providing an update on science fair status, emphasizing the limited time left and a recommended timeline for finishing the project. Dr. Garcia also mentioned the CYSF portal, stating that it is something we should remember to do, although doesn't hold precedence over our other work, considering that if we don't make the city science fair, we won't need to complete it, and even if we do progress, we would still have another week and a half to complete it.

This evening, I also worked on preparing my logbook and background research for the science fair. Recognizing that a significant portion of my background research on APOE would now be obsolete, and also that my research was bulleted and disorganized, I created a new section, documenting my research in a more coherent and formal way.

January 24, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 (Postponed) ☐ Clean the CSF and Master File for Thursday (New)	None	1. Meeting with Bhavana and Britney today at 1:00 PM

Review

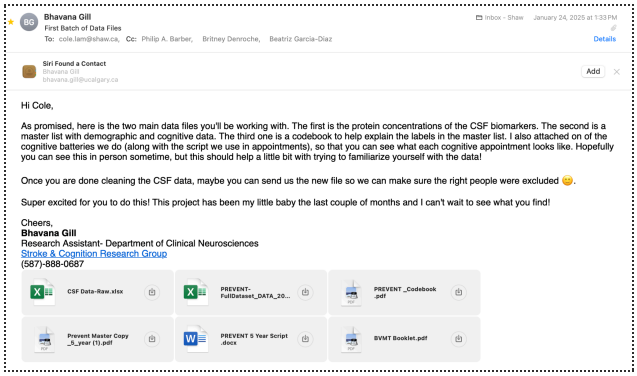
This afternoon, I had my meeting with Bhavana and Britney, discussing changes to the project, along with the path forward with data collection and statistical analysis. I also talked to Dr. Garcia to get an extension on my research paper introduction given the abrupt changes.

Notes:

- Changes to the project:
  - APOE → CSF
    - How can I draw associations between CSF and CSVD?
  - CSVD and MRIs?
  - Data: lumbar punctures → CSF
    - Total sample size: <100
  - Data collection:
    - 1. Only keep people with full data sets (80 something)
      - Some people don't have certain values entered for certain protein levels
      - WE NEED ALL PROTEIN LEVELS
        - P-tau
        - T-tau
        - AB-42 → might be a better predictor
        - AB-40
          - Started to be analyzed later, so many participants are missing it
        - Ratio of ab42/ab40
        - Ratio of ab42/p-tau
      - CSF data provides insight in to AD biomarkers
        - Not been analyzed in TIA participants because CSF data collection is rarer
    - 2. Statistical analyses
      - Is there a difference in the four protein levels?
      - Regression analysis: does group status predict levels of ____?
        - Controls: age, sex? (not too significant)
    - Big data file:
      - CSF members have ID numbers
        - Delete all members without CSF
    - SPSS software for analyzing statistical analyses
      - Not free…
    - Free: Jasp
    - Also should report of mean level of education and other demographics
  - **Starting point:**
    - CSF files to clean
    - Other master file to clean

- Ways to do the second part:
  - Cross sectional analysis (time close to lumbar puncture and cognitive tests)
- Part 2 of project?:
  - Comparing CSF data to cognitive data
  - If TIAs have higher biomarker levels, does it also correlate to more impairment/subtle declines in cognition?
    - They have lots of cognitive data
  - Methods:
    - 1. Look at CSF data
    - 2. Look at group differences
    - 3. Group regressions
- Next Meeting:
  - Thursday, January 30 at 10:30 AM

After the meeting, Bhavana sent me an email with the CSF file and the master file. Britney sent the link for the next meeting on Thursday, and I sent a confirmation email that I received the data, and also asked about whether the University of Calgary could grant me an SPSS license.



Bhavana Gill
First Batch of Data Files
To: cole.lam@shaw.ca, Cc: Philip A. Barber, Britney Denroche, Beatriz Garcia-Diaz
Inbox - Shaw January 24, 2025 at 1:33 PM
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

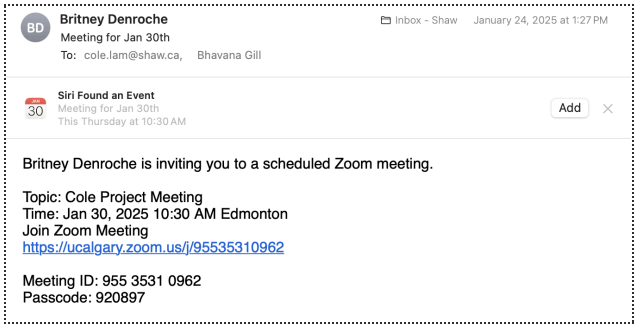
As promised, here is the two main data files you'll be working with. The first is the protein concentrations of the CSF biomarkers. The second is a master list with demographic and cognitive data. The third one is a codebook to help explain the labels in the master list. I also attached on of the cognitive batteries we do (along with the script we use in appointments), so that you can see what each cognitive appointment looks like. Hopefully you can see this in person sometime, but this should help a little bit with trying to familiarize yourself with the data!

Once you are done cleaning the CSF data, maybe you can send us the new file so we can make sure the right people were excluded 😔.

Super excited for you to do this! This project has been my little baby the last couple of months and I can't wait to see what you find!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

CSF Data-Raw.xlsx
PREVENT-FullDataset_DATA_20...
PREVENT _Codebook .pdf
Prevent Master Copy _5_year (1).pdf
PREVENT 5 Year Script .docx
BVMT Booklet.pdf



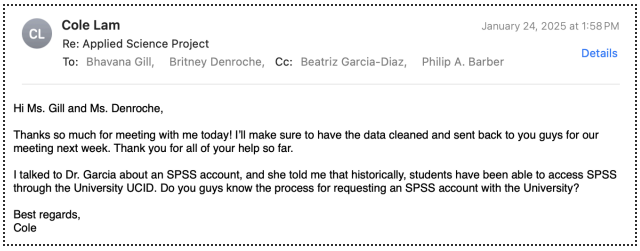
Britney Denroche
Meeting for Jan 30th
To: cole.lam@shaw.ca, Bhavana Gill
Inbox - Shaw January 24, 2025 at 1:27 PM

Siri Found an Event
Meeting for Jan 30th
This Thursday at 10:30 AM
Add

Britney Denroche is inviting you to a scheduled Zoom meeting.

Topic: Cole Project Meeting
Time: Jan 30, 2025 10:30 AM Edmonton
Join Zoom Meeting
https://ucalgary.zoom.us/j/95535310962

Meeting ID: 955 3531 0962
Passcode: 920897



Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Britney Denroche, Cc: Beatriz Garcia-Diaz, Philip A. Barber
January 24, 2025 at 1:58 PM
Details

Hi Ms. Gill and Ms. Denroche,

Thanks so much for meeting with me today! I'll make sure to have the data cleaned and sent back to you guys for our meeting next week. Thank you for all of your help so far.

I talked to Dr. Garcia about an SPSS account, and she told me that historically, students have been able to access SPSS through the University UCID. Do you guys know the process for requesting an SPSS account with the University?

Best regards,
Cole

January 26, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 (Postponed) ☐ Clean the CSF and Master File for Thursday	None	1. Meeting with Bhavana and Britney tomorrow at 1:00 PM

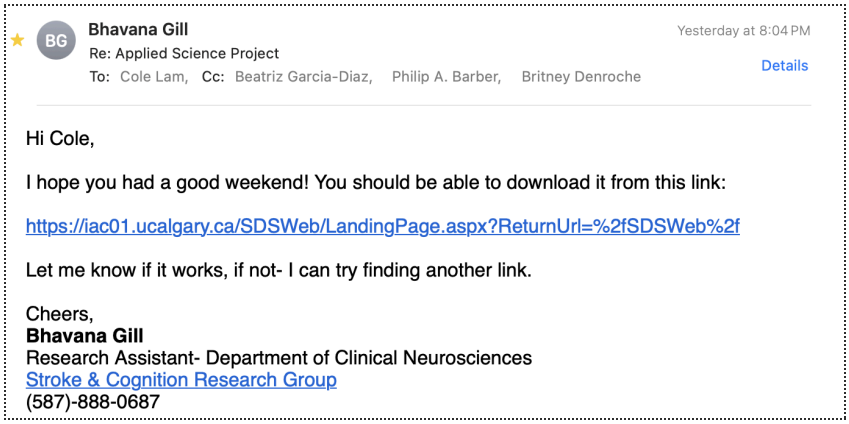
Review

This day, I started cleaning the data for the CSF file. I created a copy of the CSF file, and then went through each variable to make sense of what each one was referring to. I also looked at the conditional formatting to establish what values were considered abnormal in the initial formatting. For instance, values below 620 ng/L for Aβ 1-42 are considered abnormal and correlate with AD.

My cleaning process (CSF File):

1. Fixed structural errors and inconsistent labelling
2. Created common labels between the data from both sheets in the CSF spreadsheet

Bhavana also responded by sending me a link for requesting an SPSS license, and I responded confirming that I sent the request, and also clarified to see if there was any “bad data” that needed to be cleaned other than incomplete data.



Bhavana Gill Yesterday at 8:04 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Hi Cole,

I hope you had a good weekend! You should be able to download it from this link:

https://iac01.ucalgary.ca/SDSWeb/LandingPage.aspx?ReturnUrl=%2fSDSWeb%2f

Let me know if it works, if not- I can try finding another link.

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam Yesterday at 8:33 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Thanks so much for the link, Ms. Gill!

I sent an email to IT via your URL to request an SPSS license, and CCed you, Ms. Denroche, and Dr. Barber. Hopefully they can grant me an account, although my email didn't appear in my Sent mailbox so I hope it properly sent…

On a separate note, I looking through the data this weekend and did some organizing just for my sake. Just hoped to clarify specifically what data constitutes as “bad data”, considering nearly all of the participants who volunteered for the lumbar puncture listed on the second spreadsheet had complete data for all four proteins and their corresponding ratios. Otherwise, if none of the data needs to be removed, there is very little cleaning to do.

Thanks so much for your help!

Best regards,
Cole

January 27, 2025

Tasks To-do

- [ ] Research Paper Introduction due Jan. 30 (Postponed)
- [ ] Clean the CSF and Master File for Thursday

Tasks Completed

None

Review

This evening, I spent some more time with the two sets of data I was sent. Because all my data for the CSF file was cleaned (all members that remained had complete data), I made sure to compare the patient ideas and demographics between the two sheets to ensure consistency. Specifically, I also added some columns that allowed me to filter the data to only include individuals who had the lumbar puncture completed, and also for individuals who had the complete data. I then cross referenced the data, and was able to confirm that the data I had filtered was consistent between the two sheets.

Notes

None

January 28, 2025

Tasks To-do

- [ ] Research Paper Introduction due Jan. 30 (Postponed)

Tasks Completed

- [x] Clean the CSF and Master File for Thursday

Review

During class time, I finished looking through all of the CSF and master file data, ensuring that it was consistent and usable for my statistical analysis. After that, I conducted more research into the role of p-tau and t-tau, and started making modifications to my introduction for my research paper. I also renamed my project to *The significance of cerebrospinal fluid protein biomarkers in predicting cognitive decline in transient ischemic attack patients compared with healthy controls*, which I could potentially modify later. I took out all of the information about the APOE, CSVD, and MRIs, and added information about the importance of preventing cognitive decline, and bulked up the section talking about how valuable analyzing TIAs can be. I then added a section about lumbar punctures and CSF, and provided some details about how the protein levels vary between healthy controls and demented patients to establish what I would be looking for. Lastly, I revised the objectives and summary section for the entire project, emphasizing the two parts of the project (how does CSF compared between TIA patients and controls; do the protein concentrations impact cognition) and relating it to the big goal of corroborating evidence that TIA is a valuable predictor of future cognitive decline.

Notes

January 29, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 (Postponed)	None	1. Meeting with Bhavana and Britney tomorrow at 10:30 AM

Review

In anticipation of getting more detailed information about the data analysis during the next meeting, I preemptively downloaded the free JASP statistical analysis software, considering that IT at the University of Calgary was not responding to my request for an SPSS license. I took my CSF data and uploaded it into the newly downloaded JASP software, made modifications where they were necessary (variable types, titles, naming inconsistencies), and then got the program to create some summaries of the data. Although I wasn't sure what to do with it right away, it was valuable in better understanding the general results of the data, and the trends that I should expect to see upon more advanced statistical analysis.

Results

Descriptive Statistics

Descriptive Statistics

	T-tau (ng/L)		P-tau (ng/L)		Aβ1-40 (ng/l)		Aβ1-42 (ng/L)	
	TIA	control	TIA	control	TIA	control	TIA	control
Valid	19	30	19	30	19	30	19	30
Missing	0	0	0	0	0	0	0	0
Mean	389.211	346.233	49.300	44.800	9937.526	10300.867	869.368	1024.567
Std. Deviation	218.051	173.799	30.670	17.924	2768.224	2436.329	279.458	302.606
Minimum	89.000	132.000	17.300	21.600	4743.000	5247.000	414.000	384.000
Maximum	893.000	835.000	148.700	107.200	17245.000	17642.000	1294.000	1789.000

Note. Excluded 9 rows from the analysis that correspond to the missing values of the split-by variable diagnosis

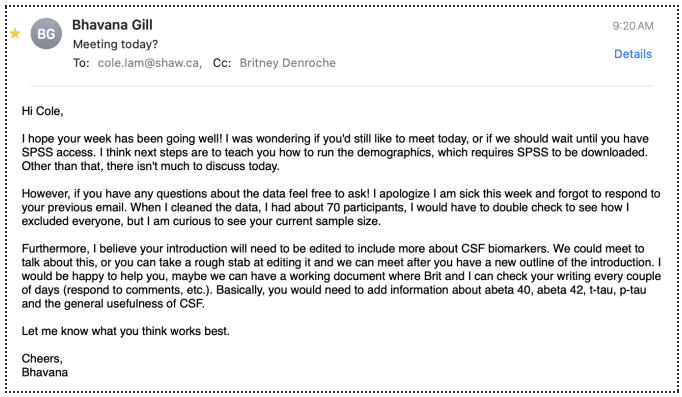
In analyzing the descriptive statistical summary here, my first impressions of the data were that the Aβ values between TIAs and controls vary significantly more than with regard to tau. Both t-tau and p-tau have similar means, standard deviations, and minimum and maximum values. Compared to the Aβ concentrations, values for TIA patients were more consistent with existing trends of AD and related dementia patients. That is, Aβ42 and Aβ40 were lower than in healthy controls. Obviously, no nuanced conclusions can be made solely with this data, but it was a great first impression upon inputting the data.

January 30, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 (Postponed)	None	1. Meeting with Bhavana and Britney today at 10:30 AM

Review

This morning, Bhavana emailed to clarify if I still thought it would be good to meet. Because I didn't have the SPSS software, it would be hard to continue doing any work. I responded saying that it would still be great to better understand the next steps, and that I could try and follow using JASP. Because Britney was unavailable, my meeting with Bhavana started at 10:30 AM.



Bhavana Gill 9:20 AM
Meeting today?
To: cole.lam@shaw.ca, Cc: Britney Denroche Details

Hi Cole,

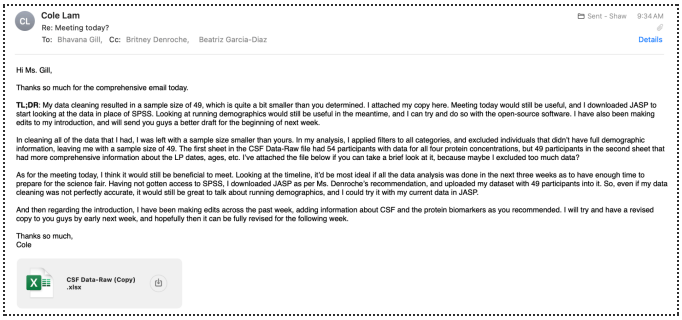
I hope your week has been going well! I was wondering if you'd still like to meet today, or if we should wait until you have SPSS access. I think next steps are to teach you how to run the demographics, which requires SPSS to be downloaded. Other than that, there isn't much to discuss today.

However, if you have any questions about the data feel free to ask! I apologize I am sick this week and forgot to respond to your previous email. When I cleaned the data, I had about 70 participants, I would have to double check to see how I excluded everyone, but I am curious to see your current sample size.

Furthermore, I believe your introduction will need to be edited to include more about CSF biomarkers. We could meet to talk about this, or you can take a rough stab at editing it and we can meet after you have a new outline of the introduction. I would be happy to help you, maybe we can have a working document where Brit and I can check your writing every couple of days (respond to comments, etc.). Basically, you would need to add information about abeta 40, abeta 42, t-tau, p-tau and the general usefulness of CSF.

Let me know what you think works best.

Cheers,
Bhavana



Cole Lam Sent - Shaw 9:34 AM
Re: Meeting today?
To: Bhavana Gill, Cc: Britney Denroche, Beatriz Garcia-Diaz Details

Hi Ms. Gill,

Thanks so much for the comprehensive email today.

TL;DR: My data cleaning resulted in a sample size of 49, which is quite a bit smaller than you determined. I attached my copy here. Meeting today would still be useful, and I downloaded JASP to start looking at the data in place of SPSS. Looking at running demographics would still be useful in the meantime, and I can try and do so with the open-source software. I have also been making edits to my introduction, and will send you guys a better draft for the beginning of next week.

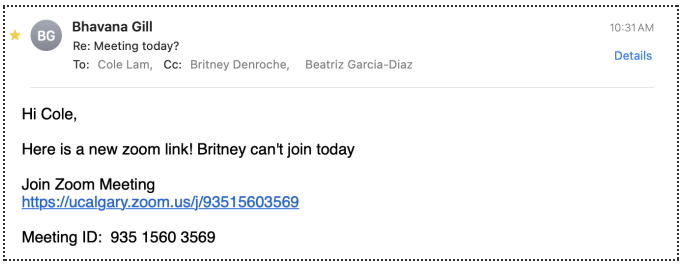
In cleaning all of the data that I had, I was left with a sample size smaller than yours. In my analysis, I applied filters to all categories, and excluded individuals that didn't have full demographic information, leaving me with a sample size of 49. The first sheet in the CSF Data-Raw file had 54 participants with data for all four protein concentrations, but 49 participants in the second sheet that had more comprehensive information about the LP dates, ages, etc. I've attached the file below if you can take a brief look at it, because maybe I excluded too much data?

As for the meeting today, I think it would still be beneficial to meet. Looking at the timeline, it'd be most ideal if all the data analysis was done in the next three weeks as to have enough time to prepare for the science fair. Having not gotten access to SPSS, I downloaded JASP as per Ms. Denroche's recommendation, and uploaded my dataset with 49 participants into it. So, even if my data cleaning was not perfectly accurate, it would still be great to talk about running demographics, and I could try it with my current data in JASP.

And then regarding the introduction, I have been making edits across the past week, adding information about CSF and the protein biomarkers as you recommended. I will try and have a revised copy to you guys by early next week, and hopefully then it can be fully revised for the following week.

Thanks so much,
Cole

CSF Data-Raw (Copy) .xlsx



Bhavana Gill 10:31 AM
Re: Meeting today?
To: Cole Lam, Cc: Britney Denroche, Beatriz Garcia-Diaz Details

Hi Cole,

Here is a new zoom link! Britney can't join today

Join Zoom Meeting
https://ucalgary.zoom.us/j/93515603569

Meeting ID: 935 1560 3569

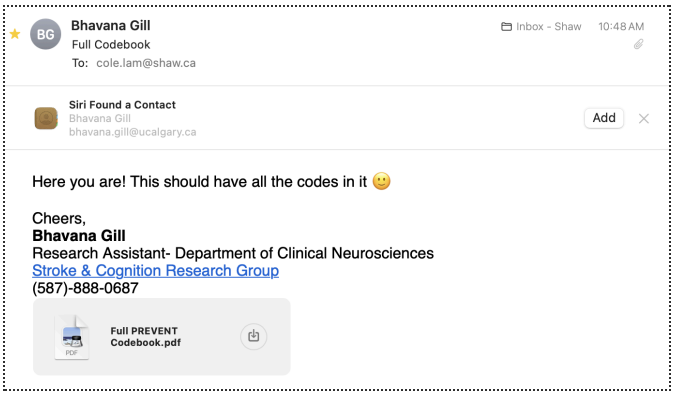
Notes:

- Master File Key:
  - It looks like the PDF sent had some of the categories collapsed, so for demographics such as race, education, etc., I could not determine what those values were…
- Data cleaning:
  - Because Aβ40 was assessed in later patients, we shouldn't use it as exclusion criteria. Only

sorting out individuals who are missing one or more of t-tau, p-tau, and Aβ42 should be filtered out.

- Demographics:
    - Male to female
    - TIA to controls
    - Age
- Data analysis software:
    - Bhavana wasn't the most familiar with JASP, so we are going to wait to get SPSS access.

I then sent a summary email, providing all my available dates for February so that once I was able to get SPSS software, we could immediately proceed. Bhavana also sent me the complete codebook.



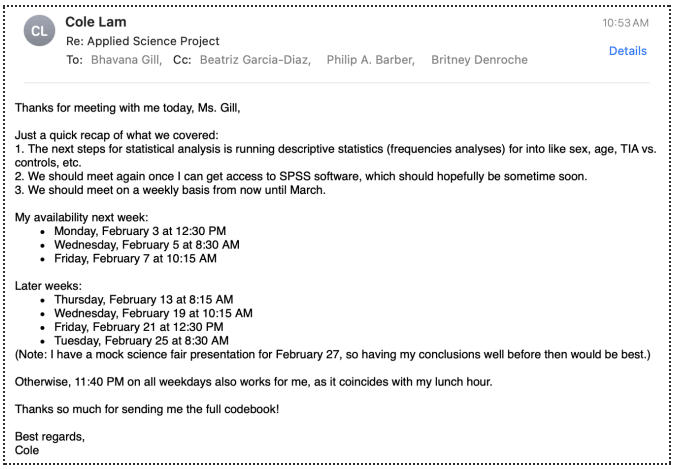
Bhavana Gill — Inbox – Shaw 10:48 AM
Full Codebook
To: cole.lam@shaw.ca

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Here you are! This should have all the codes in it 🙂

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Full PREVENT Codebook.pdf



Cole Lam 10:53 AM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche
Details

Thanks for meeting with me today, Ms. Gill,

Just a quick recap of what we covered:
1. The next steps for statistical analysis is running descriptive statistics (frequencies analyses) for into like sex, age, TIA vs. controls, etc.
2. We should meet again once I can get access to SPSS software, which should hopefully be sometime soon.
3. We should meet on a weekly basis from now until March.

My availability next week:
- Monday, February 3 at 12:30 PM
- Wednesday, February 5 at 8:30 AM
- Friday, February 7 at 10:15 AM

Later weeks:
- Thursday, February 13 at 8:15 AM
- Wednesday, February 19 at 10:15 AM
- Friday, February 21 at 12:30 PM
- Tuesday, February 25 at 8:30 AM

(Note: I have a mock science fair presentation for February 27, so having my conclusions well before then would be best.)

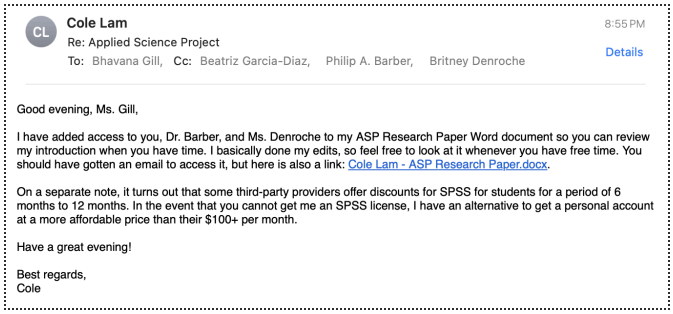
Otherwise, 11:40 PM on all weekdays also works for me, as it coincides with my lunch hour.

Thanks so much for sending me the full codebook!

Best regards,
Cole

For the rest of class, I went back through all the data sets and revised the members I excluded due to not having Aβ40 data. I also made revisions to my introduction and added details to my methodology section of my final research paper.

This evening, I updated access to my research paper document so that Dr. Barber, Bhavana, and Britney could review it when they had time. I also advised Bhavana about the discounted SPSS account that I could get in place of a license via the University of Calgary.



Cole Lam 8:55 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche
Details

Good evening, Ms. Gill,

I have added access to you, Dr. Barber, and Ms. Denroche to my ASP Research Paper Word document so you can review my introduction when you have time. I basically done my edits, so feel free to look at it whenever you have free time. You should have gotten an email to access it, but here is also a link: Cole Lam - ASP Research Paper.docx.

On a separate note, it turns out that some third-party providers offer discounts for SPSS for students for a period of 6 months to 12 months. In the event that you cannot get me an SPSS license, I have an alternative to get a personal account at a more affordable price than their $100+ per month.

Have a great evening!

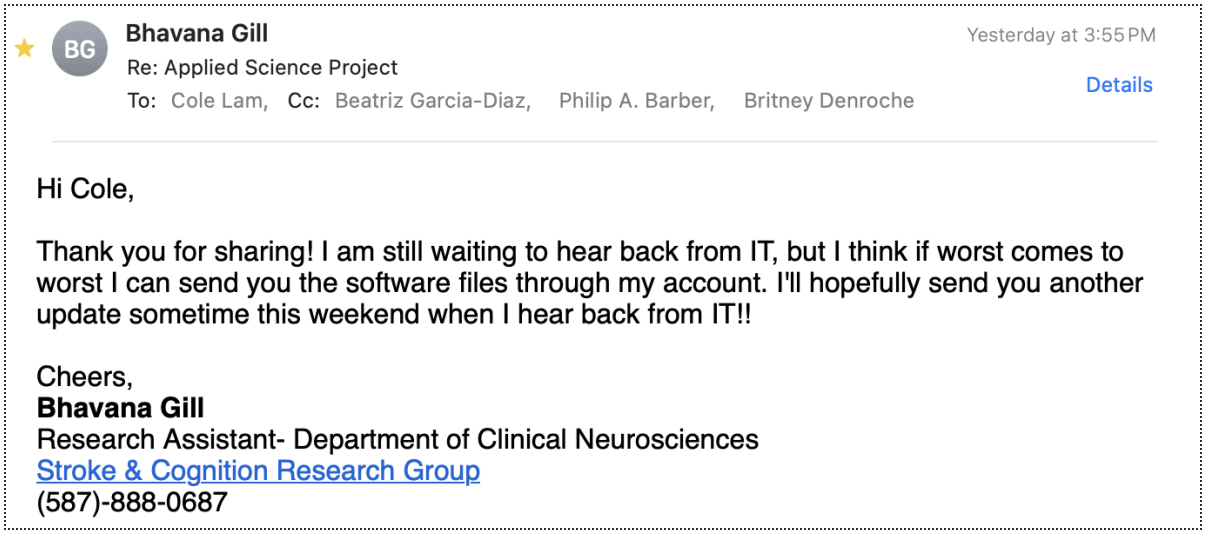
Best regards,
Cole

January 31, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Jan. 30 (Postponed)	None	None

Review

This afternoon, Bhavana sent me an email in response to me sending her my research paper, mentioning that IT had yet to respond to her request to get me an SPSS license, but even if she couldn't get me the license, she would send me her software files for her account.



Bhavana Gill Yesterday at 3:55 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Hi Cole,

Thank you for sharing! I am still waiting to hear back from IT, but I think if worst comes to worst I can send you the software files through my account. I'll hopefully send you another update sometime this weekend when I hear back from IT!!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Daily Notes

February 1, 2025

Tasks To-do

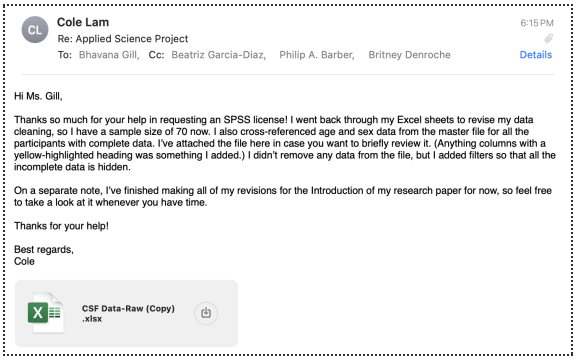
- [ ] Research Paper Introduction due Jan. 30 (Postponed)

Tasks Completed

None

Review

In order to make sure all of my background research was completed in time for the science fair, I spent a lot of time this afternoon adding details to my Research (Final) document. Specifically, I added lots of information about CSF, tau proteins, Aβ proteins, and lumbar punctures. I also spent some time updating my CYSF portal, filling out the “Problem” section with excerpts from my research paper Introduction.
In the evening, I made my final revisions to my research paper before I asked Bhavana to review it. I also finished reviewing my data cleaning. Then, I sent an email to Bhavana and Britney, mentioning that I finished fixing the data (and attached it) and also noting that my edits for my introduction were done and ready for review.



Cole Lam 6:15 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Hi Ms. Gill,

Thanks so much for your help in requesting an SPSS license! I went back through my Excel sheets to revise my data cleaning, so I have a sample size of 70 now. I also cross-referenced age and sex data from the master file for all the participants with complete data. I've attached the file here in case you want to briefly review it. (Anything columns with a yellow-highlighted heading was something I added.) I didn't remove any data from the file, but I added filters so that all the incomplete data is hidden.

On a separate note, I've finished making all of my revisions for the Introduction of my research paper for now, so feel free to take a look at it whenever you have time.

Thanks for your help!

Best regards,
Cole

CSF Data-Raw (Copy) .xlsx

Notes

None

February 3, 2025

Tasks To-do

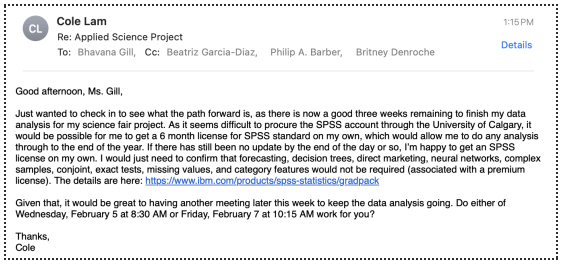
- [ ] Research Paper Introduction due Jan. 30 (Postponed)

Tasks Completed

None

Review

Dr. Garcia, during class, spent a lot of time mentioning the quality of the logbooks and what we need to do overall preparing for the science fair. She emphasized the importance of keeping up with our data analysis and recording it, either in a unique section of our logbook, or in our Daily Notes section. I also sent another email to Bhavana seeing if we could meet again soon to continue with data analysis. I made sure to mention that there were student offers to get a cheaper SPSS license that I could procure given that IT at the University of Calgary was taking a long time.



CL **Cole Lam** 1:15 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Good afternoon, Ms. Gill,

Just wanted to check in to see what the path forward is, as there is now a good three weeks remaining to finish my data analysis for my science fair project. As it seems difficult to procure the SPSS account through the University of Calgary, it would be possible for me to get a 6 month license for SPSS standard on my own, which would allow me to do any analysis through to the end of the year. If there has still been no update by the end of the day or so, I'm happy to get an SPSS license on my own. I would just need to confirm that forecasting, decision trees, direct marketing, neural networks, complex samples, conjoint, exact tests, missing values, and category features would not be required (associated with a premium license). The details are here: https://www.ibm.com/products/spss-statistics/gradpack

Given that, it would be great to having another meeting later this week to keep the data analysis going. Do either of Wednesday, February 5 at 8:30 AM or Friday, February 7 at 10:15 AM work for you?

Thanks,
Cole

Notes

None

February 4, 2025

Tasks To-do

- [ ] Research Paper Introduction due Jan. 30 (Postponed)

Tasks Completed

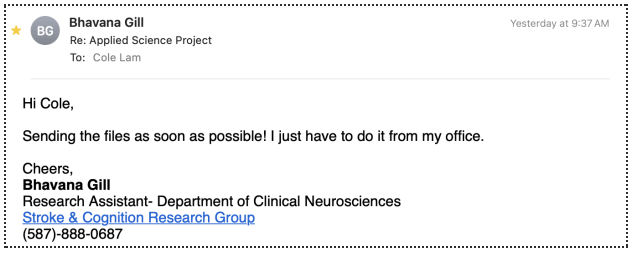
None

Notes

None

Review

Throughout the day, Bhavana sent me the files for downloaded SPSS 29 onto my laptop. She gave me her authorization code; however, after downloading the software, the authorization code did not let me access the license. I sent an email mentioning this, and she replied by saying that she would call IT to figure out the problem.



BG **Bhavana Gill** Yesterday at 9:37 AM
Re: Applied Science Project
To: Cole Lam

Hi Cole,

Sending the files as soon as possible! I just have to do it from my office.

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Bhavana Gill Yesterday at 12:45 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz Details

Hi Cole,

Please see the attached files. The "Read me" should contain a step by step guide on how to download everything 🙂. Let me know if it works! I'll send another email with two more files

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

See More from Bhavana Gill

Bhavana Gill Yesterday at 12:47 PM
Re: Applied Science Project
To: cole.lam@shaw.ca

Change in plans, the other two files are too large so I shared a folder with you titled "Cole SPSS"

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Bhavana Gill shared a folder with you

Here's the folder that Bhavana Gill shared with you.

Cole SPSS

This link only works for the direct recipients of this message.

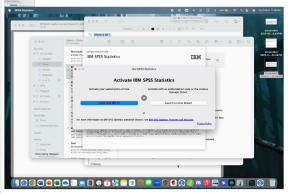
Open

UNIVERSITY OF CALGARY Start something.

Cole Lam
Re: Applied Science Project
To: Bhavana Gill
Sent - Shaw Yesterday at 2:31 PM

Thanks for the links, Ms. Gill

It doesn't seem like the Authorization Code is working for me. (I used 6f11c57e503804e797d0)



Perhaps this authorization code is no longer valid?

Best regards,
Cole

Bhavana Gill Yesterday at 3:37 PM
Re: Applied Science Project
To: Cole Lam

Hi Cole,

I will give IT a call.. It should work and doesn't usually time out.

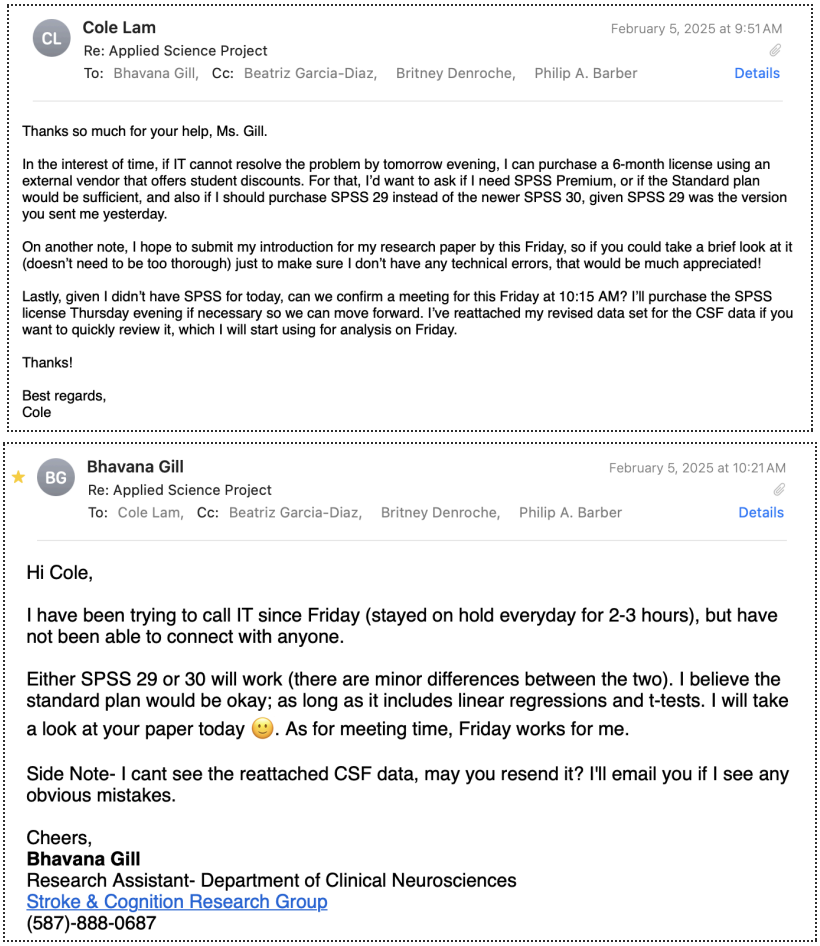
Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

February 5, 2025

Tasks To-do	Tasks Completed	Notes
☐ Research Paper Introduction due Feb. 7 (New)	None	None

Review

During class, I had a biweekly meeting with Dr. Garcia, in which we talked about how to maximize the remaining three weeks before I needed to have my science fair project completed. Because I was waiting on SPSS, Dr. Garcia recommended that I start thinking ahead in planning my poster and doing any necessary background research. I told her that I planned on purchasing an SPSS 30 Standard license this evening if Bhavana could not get the license by then, just because IT at the University of Calgary was taking too long. Otherwise, I kept working on my background research, adding details to the blood work section.



CL **Cole Lam** February 5, 2025 at 9:51 AM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber Details

Thanks so much for your help, Ms. Gill.

In the interest of time, if IT cannot resolve the problem by tomorrow evening, I can purchase a 6-month license using an external vendor that offers student discounts. For that, I'd want to ask if I need SPSS Premium, or if the Standard plan would be sufficient, and also if I should purchase SPSS 29 instead of the newer SPSS 30, given SPSS 29 was the version you sent me yesterday.

On another note, I hope to submit my introduction for my research paper by this Friday, so if you could take a brief look at it (doesn't need to be too thorough) just to make sure I don't have any technical errors, that would be much appreciated!

Lastly, given I didn't have SPSS for today, can we confirm a meeting for this Friday at 10:15 AM? I'll purchase the SPSS license Thursday evening if necessary so we can move forward. I've reattached my revised data set for the CSF data if you want to quickly review it, which I will start using for analysis on Friday.

Thanks!

Best regards,
Cole

BG **Bhavana Gill** February 5, 2025 at 10:21 AM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber Details

Hi Cole,

I have been trying to call IT since Friday (stayed on hold everyday for 2-3 hours), but have not been able to connect with anyone.

Either SPSS 29 or 30 will work (there are minor differences between the two). I believe the standard plan would be okay; as long as it includes linear regressions and t-tests. I will take a look at your paper today 🙂. As for meeting time, Friday works for me.

Side Note- I cant see the reattached CSF data, may you resend it? I'll email you if I see any obvious mistakes.

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam February 5, 2025 at 12:32 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber Details

Thanks so much for all of your help and dedication, Ms. Gill! I really appreciate the time you've put towards helping me continue with this project, despite the complications that have arisen.

I'll get an SPSS license tonight so I can familiarize myself a little bit tomorrow and Friday. Please don't worry about getting on the phone with IT again; the endeavour is probably pretty fruitless.

I've reattached the CSF data file here! Thanks so much for reviewing my paper!

Once again, thanks so much for all of our help!

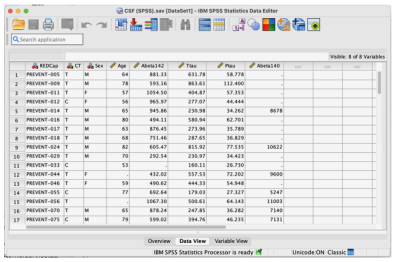
Best regards,
Cole

CSF Data-Raw (Copy) .xlsx

Cole Lam February 5, 2025 at 9:11 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber Details

Good evening, Ms. Gill,

Very sorry for the late email. Just wanted to report that I was able to purchase a discounted SPSS 30 license for academic use, and that everything has gone successfully!



I look forward to meeting you on Friday!

Best regards,
Cole

February 6, 2025

Tasks To-do

- [ ] Research Paper Introduction due Feb. 7

Tasks Completed

None

Review

This evening, I sent the Zoom link for my meeting with Bhavana.

Cole Lam February 6, 2025 at 9:39 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber Details

Good evening, Ms. Gill,

I've created a meeting for tomorrow at 10:15 AM, and I've attached the information below. I had to create it with my Webber email, which doesn't allow for sending or receiving emails external of Webber Academy, so you probably would not have gotten an email with the invite…

Because of my free account, the maximum meeting length is 40 minutes, so if we need to go beyond that, I can set up another meeting!

Join our Cloud HD Video Meeting
us05web.zoom.us

Meeting ID: 82357134838
Passcode: 0jFBF9

See you tomorrow!

Best regards,
Cole

Notes

None

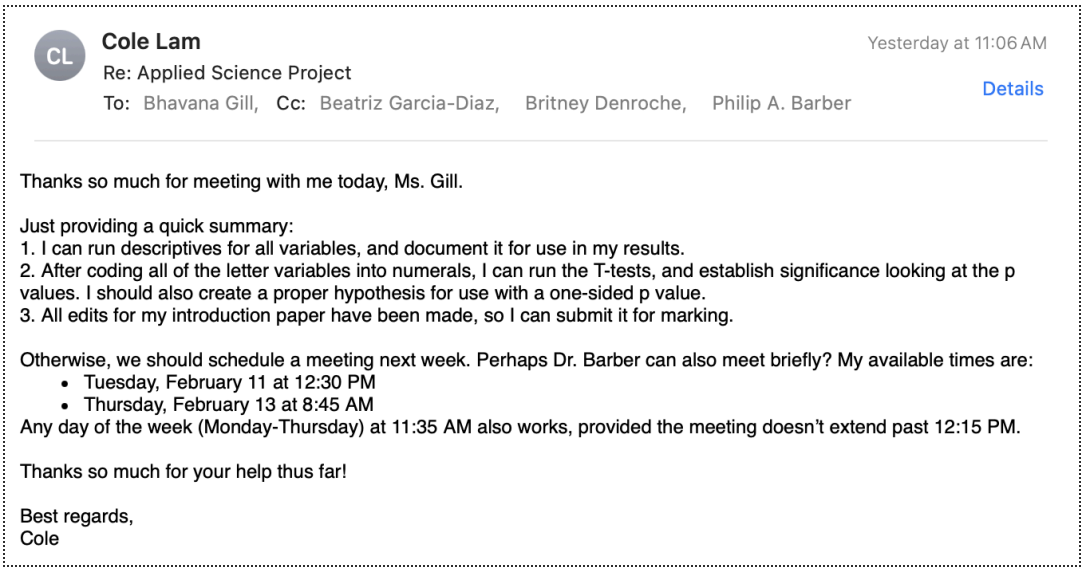
February 7, 2025

Tasks To-do	Tasks Completed	Notes
☐ Run descriptive statistics for all demographics, CSF and cognitive data (New) ☐ Run t-tests for all cognitive/CSF data comparing TIAs and controls (New) ☐ Research Paper Methodology due Feb. 19 (New)	☑ Research Paper Introduction due Feb. 7	1. We will meet again some time next week, hopefully with Dr. Barber, to clarify which cognitive tests are valuable to assess.

Review

In class, we discussed the situation with science fair meetings, considering that report cards close on February 28th at 9:00 AM. Because of this, she talked about some alternatives, and we decided that we would move everyone to Feb 25 and Feb 27, and then cram all of the presentations in then. After this, I had a meeting with Bhavana to discuss the descriptives and t-tests. Some notes included:

- Mean and SD is all we need for continuous variables (not other values like maximum and minimum)
- Our expectation is that we would see higher tau concentrations in CSF due to increased production and tangles in the brain (alternate hypothesis)
- Question for later: Confidence intervals vs. p values for Aβ42



CL **Cole Lam** Yesterday at 11:06 AM

Re: Applied Science Project

To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber Details

Thanks so much for meeting with me today, Ms. Gill.

Just providing a quick summary:
1. I can run descriptives for all variables, and document it for use in my results.
2. After coding all of the letter variables into numerals, I can run the T-tests, and establish significance looking at the p values. I should also create a proper hypothesis for use with a one-sided p value.
3. All edits for my introduction paper have been made, so I can submit it for marking.

Otherwise, we should schedule a meeting next week. Perhaps Dr. Barber can also meet briefly? My available times are:
- Tuesday, February 11 at 12:30 PM
- Thursday, February 13 at 8:45 AM

Any day of the week (Monday-Thursday) at 11:35 AM also works, provided the meeting doesn't extend past 12:15 PM.

Thanks so much for your help thus far!

Best regards,
Cole

I also submitted my final draft of my research paper introduction to Dr. Garcia and Turnitin.

February 8, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Research Paper Methodology due Feb. 19

Tasks Completed

None

Notes

None

Review

This afternoon, after updating my logbook and calendar, I started conducting some of the data analysis, running the descriptives and t-tests for the data that I had. I also compiled a list of data I was missing to send to Bhavana on Monday. I started my data analysis by coding the values for some of the nominal variables. This included the sexes (which I labelled 0: M, 1: F) and the control/treatment groups (0: control, 1: treatment). I then included all the data results that I found using the software in the Data Collection (Tables) section of this logbook. Specifically, I did the CSF descriptives and T-tests.

February 9, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Research Paper Methodology due Feb. 19

Tasks Completed

None

Review

This afternoon, I spent some more time conducting my data analysis, focusing on the cognitive data. Because Bhavana mentioned that which tests were going to be used had not yet been determined, I ran the descriptives and t-tests for all of the summary values for the major tests such as the ACE-R, BVMT, and MoCA. I also added that information to my email to send out Monday morning.

Notes

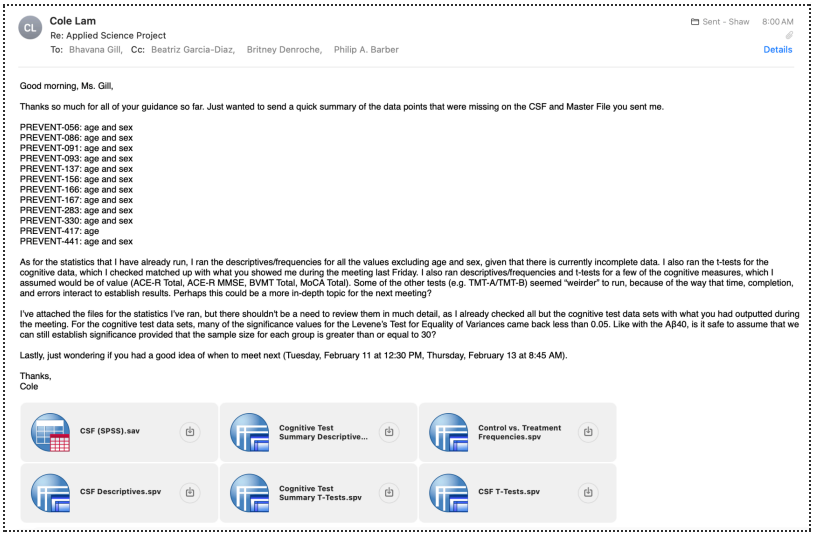
None

February 10, 2025

Tasks To-do	Tasks Completed	Notes
☐ Run descriptive statistics for all demographics, CSF and cognitive data ☐ Run t-tests for all cognitive/CSF data comparing TIAs and controls ☐ Research Paper Methodology due Feb. 19	None	None

Review

This morning, my email to Bhavana and Britney about the missing data was sent, along with an update on the cognitive assessments I ran tests for. I also asked when we should meet next to finalize the tests that I am going to run.



Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber
Sent - Shaw 8:00 AM
Details

Good morning, Ms. Gill,

Thanks so much for all of your guidance so far. Just wanted to send a quick summary of the data points that were missing on the CSF and Master File you sent me.

PREVENT-056: age and sex
PREVENT-086: age and sex
PREVENT-091: age and sex
PREVENT-093: age and sex
PREVENT-137: age and sex
PREVENT-156: age and sex
PREVENT-166: age and sex
PREVENT-167: age and sex
PREVENT-283: age and sex
PREVENT-330: age and sex
PREVENT-417: age
PREVENT-441: age and sex

As for the statistics that I have already run, I ran the descriptives/frequencies for all the values excluding age and sex, given that there is currently incomplete data. I also ran the t-tests for the cognitive data, which I checked matched up with what you showed me during the meeting last Friday. I also ran descriptives/frequencies and t-tests for a few of the cognitive measures, which I assumed would be of value (ACE-R Total, ACE-R MMSE, BVMT Total, MoCA Total). Some of the other tests (e.g. TMT-A/TMT-B) seemed "weirder" to run, because of the way that time, completion, and errors interact to establish results. Perhaps this could be a more in-depth topic for the next meeting?

I've attached the files for the statistics I've ran, but there shouldn't be a need to review them in much detail, as I already checked all but the cognitive test data sets with what you had outputted during the meeting. For the cognitive test data sets, many of the significance values for the Levene's Test for Equality of Variances came back less than 0.05. Like with the Aβ40, is it safe to assume that we can still establish significance provided that the sample size for each group is greater than or equal to 30?

Lastly, just wondering if you had a good idea of when to meet next (Tuesday, February 11 at 12:30 PM, Thursday, February 13 at 8:45 AM).

Thanks,
Cole

CSF (SPSS).sav
Cognitive Test Summary Descriptive...
Control vs. Treatment Frequencies.spv
CSF Descriptives.spv
Cognitive Test Summary T-Tests.spv
CSF T-Tests.spv

Britney responded with the missing data, which I then added to my data set. Bhavana also responded by clarifying that we should hopefully meet soon.

Britney Denroche 1:47 PM
Re: Applied Science Project
To: Cole Lam

Hi Cole,

Here are the missing age sex for the listed participants:
PREVENT-056: 75 M
PREVENT-086: 57 F
PREVENT-091: 68 F
PREVENT-093: 63 F
PREVENT-137: 64 F
PREVENT-156: 57 M
PREVENT-166: 60 M
PREVENT-167: 59 F
PREVENT-283: 66 M
PREVENT-330: 64 M
PREVENT-417: 57 F
PREVENT-441: 72 F

Kind Regards,

Britney Denroche
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(403)-483-6804

Cole Lam 4:22 PM
Re: Applied Science Project
To: Britney Denroche, Cc: Beatriz Garcia-Diaz, Bhavana Gill, Philip A. Barber
Details

Thanks so much for the prompt response, Ms. Denroche,

I'll get right to the analysis of age and sex.

Best regards,
Cole

Bhavana Gill 4:28 PM
Re: Applied Science Project
To: Cole Lam, Britney Denroche, Cc: Beatriz Garcia-Diaz, Philip A. Barber
Details

Hi Cole,

Apologies for missing your email this morning! I believe the cognitive data should be okay with regards to variance; I'll show you another way we can check that! Would you be able to meet Friday? I'll figure out the best variables to examine for the cognitive scores, as well as refresh myself on the analysis steps. Feel free to send me the updated age and sex stats; I can review that as well.

Thanks, Brit, for sending the remaining data!

Cheers,
Bhavana

Cole Lam 5:15 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Britney Denroche, Beatriz Garcia-Diaz, Philip A. Barber
Details

Hi Ms. Gill,

Thanks for the clarification! I'll send you the updated stats once I've finished updating and double-checking them. As it happens, our school has a PD day on Friday, and the Monday off as well, so it would probably be best if we could meet before then, so I'd have a fair amount of time to continue with the project. I, unfortunately, also realized that we have a school assembly tomorrow during my Applied Science class, so that makes that an infeasible time. Could either tomorrow, Wednesday or Thursday at 11:35 AM or Thursday at 8:45 AM work? If not, I can try to accommodate Friday; just send me the time.

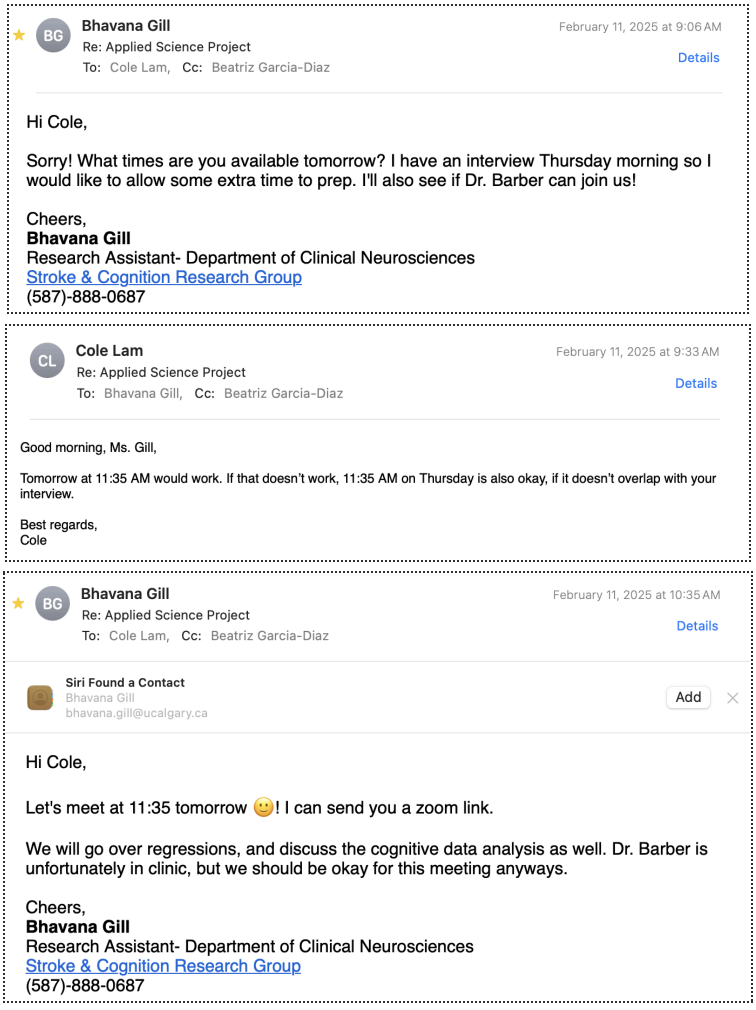
Thanks,
Cole

February 11, 2025

Tasks To-do	Tasks Completed	Notes
☐ Run descriptive statistics for all demographics, CSF and cognitive data ☐ Run t-tests for all cognitive/CSF data comparing TIAs and controls ☐ Research Paper Methodology due Feb. 19	None	1. Meeting with Bhavana at 11:35 AM tomorrow

Review

In staying in communication with Bhavana, we coordinated the times to meet next and how I should proceed with the data.



Bhavana Gill February 11, 2025 at 9:06 AM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz
Details

Hi Cole,

Sorry! What times are you available tomorrow? I have an interview Thursday morning so I would like to allow some extra time to prep. I'll also see if Dr. Barber can join us!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam February 11, 2025 at 9:33 AM
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz
Details

Good morning, Ms. Gill,

Tomorrow at 11:35 AM would work. If that doesn't work, 11:35 AM on Thursday is also okay, if it doesn't overlap with your interview.

Best regards,
Cole

Bhavana Gill February 11, 2025 at 10:35 AM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

Let's meet at 11:35 tomorrow 🙂! I can send you a zoom link.

We will go over regressions, and discuss the cognitive data analysis as well. Dr. Barber is unfortunately in clinic, but we should be okay for this meeting anyways.

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

February 12, 2025

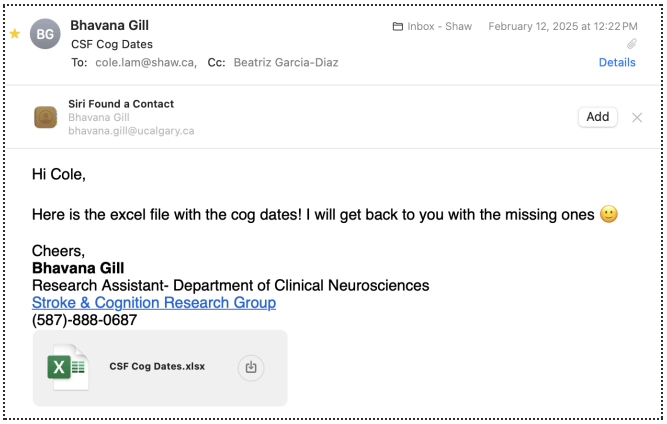
Tasks To-do	Tasks Completed	Notes
☐ Run descriptive statistics for all demographics, CSF and cognitive data ☐ Run t-tests for all cognitive/CSF data comparing TIAs and controls ☐ Research Paper Methodology due Feb. 19	None	1. Meeting with Bhavana at 11:35 AM

Review

Over the lunch hour, I spent some time talking to Bhavana about running regressions and what to do with the cognitive data tests.
Notes:

- Cross-sectional analysis for cognitive tests (LP happened at different times, so longitudinal doesn't make sense)
- MoCA and ACE-R for cognitive tests (explain this)
    - MoCA is most common screening measure used in clinics
    - ACE-R: tests the same as the MoCA but is more sensitive and accurate
- Regressions:
    - Why not moderate sex?
        - There are not consistent findings about whether there are sex differences.
    - Marginal significance: some are almost 0.05 or lower
- Inconsistencies in Aβ:
    - Regressions look at the two groups and says there isn't enough of a difference attributable to ONLY group status
        - Also accounts for age and holds it constant
    - T-test shows there are significant differences between the groups, but cannot attribute the differences to anything
- For reporting data, include the B, T, and significance values

After the meeting, Bhavana also sent me the dates for the cognitive tests that I could use for running the descriptives, t-tests, and regressions for the cognitive tests.



February 13, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Research Paper Methodology due Feb. 19

Tasks Completed

None

Review

This evening, I continued to finalize my background research for submission on Turnitin. I finished making edits to the CSF and TIA sections, updating the known trends regarding tau and Aβ concentrations. I also looked through all the data again, making sure there was consistency, and ran the statistics again to see if there were changes from updating the data. After this, I spent a fair amount of time writing my methodology section of my research paper. I tried to keep the section about the PREVENT study methods pretty brief, because it wasn't my actual methods, but when it came to writing the statistical analysis, I found that the length was quite short.

Notes

None

February 15, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Research Paper Methodology due Feb. 19

Tasks Completed

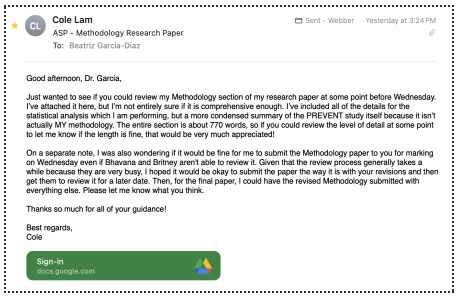
None

Notes

None

Review

This afternoon, I made some finished edits on the Methodology section of my research paper. This involved providing some more specific information about the data cleaning, what data was used, the ratios analyzed, and all of the tests used on the data. I also made sure to specify the circumstances with the marginally significant 0.056 p-values that were most likely a variable from a small sample size. I then emailed Dr. Garcia to see if she could review the paper before Feb. 19, and if it was okay for me to submit it without thorough review by my mentors until a later date.



Cole Lam
ASP - Methodology Research Paper
To: Beatriz Garcia-Diaz
Sent - Webber Yesterday at 3:24 PM

Good afternoon, Dr. Garcia,

Just wanted to see if you could review my Methodology section of my research paper at some point before Wednesday. I've attached it here, but I'm not entirely sure if it is comprehensive enough. I've included all of the details for the statistical analysis which I am performing, but a more condensed summary of the PREVENT study itself because it isn't actually MY methodology. The entire section is about 770 words, so if you could review the level of detail at some point to let me know if the length is fine, that would be very much appreciated!

On a separate note, I was also wondering if it would be fine for me to submit the Methodology paper to you for marking on Wednesday even if Bhavana and Britney aren't able to review it. Given that the review process generally takes a while because they are very busy, I hoped it would be okay to submit the paper the way it is with your revisions and then get them to review it for a later date. Then, for the final paper, I could have the revised Methodology submitted with everything else. Please let me know what you think.

Thanks so much for all of your guidance!

Best regards,
Cole

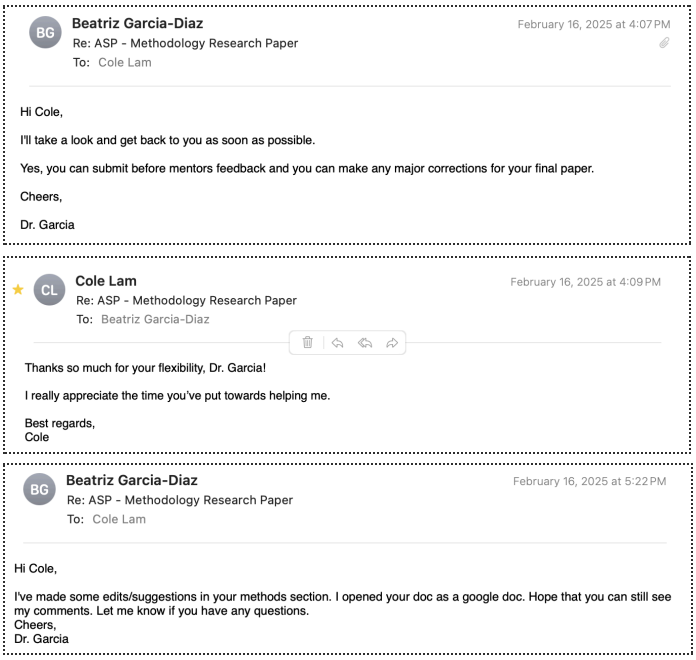
Sign-in
docs.google.com

February 16, 2025

Tasks To-do	Tasks Completed	Notes
☐ Run descriptive statistics for all demographics, CSF and cognitive data ☐ Run t-tests for all cognitive/CSF data comparing TIAs and controls ☐ Research Paper Methodology due Feb. 19	None	None

Review

This afternoon, Dr. Garcia responded to my email mentioning that she would review my methods paper as soon as she could, and that I could get my mentors to review the accuracy at a later date to get it in for the actual due date.



Beatriz Garcia-Diaz February 16, 2025 at 4:07 PM
Re: ASP - Methodology Research Paper
To: Cole Lam

Hi Cole,

I'll take a look and get back to you as soon as possible.

Yes, you can submit before mentors feedback and you can make any major corrections for your final paper.

Cheers,

Dr. Garcia

Cole Lam February 16, 2025 at 4:09 PM
Re: ASP - Methodology Research Paper
To: Beatriz Garcia-Diaz

Thanks so much for your flexibility, Dr. Garcia!

I really appreciate the time you've put towards helping me.

Best regards,
Cole

Beatriz Garcia-Diaz February 16, 2025 at 5:22 PM
Re: ASP - Methodology Research Paper
To: Cole Lam

Hi Cole,

I've made some edits/suggestions in your methods section. I opened your doc as a google doc. Hope that you can still see my comments. Let me know if you have any questions.
Cheers,
Dr. Garcia

When Dr. Garcia sent back the edits later this evening, I fixed the errors, which were largely centered around clarifying vague statements and reducing repetitive wording. She also helped me correct my reference to SPSS 30 software. Lastly, I double-checked all of my data and statistical analyses, in which everything was complete and consistent with the exception of the missing cognitive data which I was still waiting for.

February 18, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Research Paper Methodology due Feb. 19
- [ ] Complete Science Fair Poster and Presentation (New)

Tasks Completed

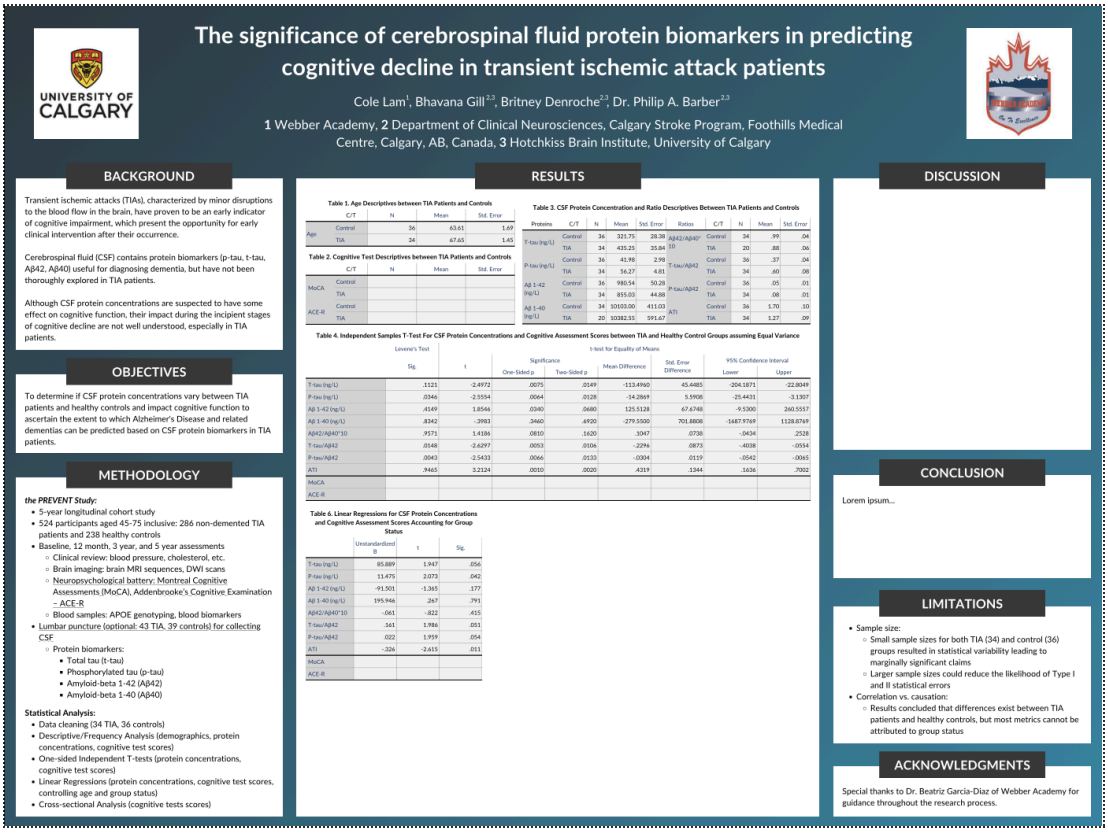
None

Notes

None

Review

This evening, I spent some time making my final revisions to my Methodology section of my research paper, fixing any grammatical errors and adding final clarifying comments. I also then started working on my science fair poster, completing the background, objectives, and methods section to the best of my abilities. Although I tried to keep word count down, I still ended up with a pretty small font, which I would plan to edit later. I also started transcribing the SPSS data onto the poster, creating my own tables to maximize the use of space.



The significance of cerebrospinal fluid protein biomarkers in predicting cognitive decline in transient ischemic attack patients

Cole Lam[1], Bhavana Gill[2,3], Britney Denroche[2,3], Dr. Philip A. Barber[2,3]

1 Webber Academy, 2 Department of Clinical Neurosciences, Calgary Stroke Program, Foothills Medical Centre, Calgary, AB, Canada, 3 Hotchkiss Brain Institute, University of Calgary

BACKGROUND

Transient ischemic attacks (TIAs), characterized by minor disruptions to the blood flow in the brain, have proven to be an early indicator of cognitive impairment, which present the opportunity for early clinical intervention after their occurrence.

Cerebrospinal fluid (CSF) contains protein biomarkers (p-tau, t-tau, Aβ42, Aβ40) useful for diagnosing dementia, but have not been thoroughly explored in TIA patients.

Although CSF protein concentrations are suspected to have some effect on cognitive function, their impact during the incipient stages of cognitive decline are not well understood, especially in TIA patients.

OBJECTIVES

To determine if CSF protein concentrations vary between TIA patients and healthy controls and impact cognitive function to ascertain the extent to which Alzheimer's Disease and related dementias can be predicted based on CSF protein biomarkers in TIA patients.

METHODOLOGY

the PREVENT Study:

- 5-year longitudinal cohort study
- 524 participants aged 45-75 inclusive: 286 non-demented TIA patients and 238 healthy controls
- Baseline, 12 month, 3 year, and 5 year assessments
  - Clinical review: blood pressure, cholesterol, etc.
  - Brain imaging: brain MRI sequences, DWI scans
  - Neuropsychological battery: Montreal Cognitive Assessments (MoCA), Addenbrooke's Cognitive Examination – ACE-R
  - Blood samples: APOE genotyping, blood biomarkers
- Lumbar puncture (optional: 43 TIA, 39 controls) for collecting CSF
  - Protein biomarkers:
    - Total tau (t-tau)
    - Phosphorylated tau (p-tau)
    - Amyloid-beta 1-42 (Aβ42)
    - Amyloid-beta 1-40 (Aβ40)

Statistical Analysis:

- Data cleaning (34 TIA, 36 controls)
- Descriptive/Frequency Analysis (demographics, protein concentrations, cognitive test scores)
- One-sided Independent T-tests (protein concentrations, cognitive test scores)
- Linear Regressions (protein concentrations, cognitive test scores, controlling age and group status)
- Cross-sectional Analysis (cognitive tests scores)

RESULTS

Table 1. Age Descriptives between TIA Patients and Controls

	C/T	N	Mean	Std. Error
Age	Control	36	63.61	1.69
	TIA	34	67.65	1.45

Table 2. Cognitive Test Descriptives between TIA Patients and Controls

	C/T	N	Mean	Std. Error
MoCA	Control			
	TIA			
ACE-R	Control			
	TIA			

Table 3. CSF Protein Concentration and Ratio Descriptives Between TIA Patients and Controls

Proteins	C/T	N	Mean	Std. Error	Ratios	C/T	N	Mean	Std. Error
T-tau (ng/L)	Control	34	321.75	28.38	Aβ42/Aβ40*10	Control	34	.99	.04
	TIA	34	431.25	33.84		TIA	20	.88	.06
P-tau (ng/L)	Control	36	41.98	2.98	T-tau/Aβ42	Control	36	.37	.04
	TIA	34	56.27	4.81		TIA	34	.60	.08
Aβ 1-42 (ng/L)	Control	36	980.54	50.28	P-tau/Aβ42	Control	36	.05	.01
	TIA	34	855.03	44.88		TIA	34	.08	.01
Aβ 1-40 (ng/L)	Control	34	10100.00	411.03	ATI	Control	36	1.70	.10
	TIA	20	10382.55	591.67		TIA	34	1.27	.09

Table 4. Independent Samples T-Test For CSF Protein Concentrations and Cognitive Assessment Scores between TIA and Healthy Control Groups assuming Equal Variance

	Levene's Test	t-test for Equality of Means						
	Sig.	t	Significance One-Sided p	Significance Two-Sided p	Mean Difference	Std. Error Difference	95% Confidence Interval Lower	95% Confidence Interval Upper
T-tau (ng/L)	.1121	-2.4972	.0075	.0149	-113.4960	45.4485	-204.1871	-22.8049
P-tau (ng/L)	.0346	-2.5554	.0064	.0128	-14.2869	5.5908	-25.4431	-3.1307
Aβ 1-42 (ng/L)	.4149	1.8546	.0340	.0680	125.5128	67.6748	-9.5300	260.5557
Aβ 1-40 (ng/L)	.8342	-.3983	.3460	.6920	-279.5500	701.8808	-1687.9769	1128.8769
Aβ42/Aβ40*10	.9571	1.4186	.0810	.1620	.1047	.0738	-.0434	.2528
T-tau/Aβ42	.0148	-2.6297	.0053	.0106	-.2296	.0873	-.4038	-.0554
P-tau/Aβ42	.0043	-2.9433	.0066	.0133	-.0304	.0119	-.0542	-.0065
ATI	.9465	3.2124	.0010	.0020	.4319	.1344	.1636	.7002
MoCA								
ACE-R								

Table 6. Linear Regressions for CSF Protein Concentrations and Cognitive Assessment Scores Accounting for Group Status

	Unstandardized B	t	Sig.
T-tau (ng/L)	85.889	1.947	.056
P-tau (ng/L)	11.475	2.073	.042
Aβ 1-42 (ng/L)	-91.501	-1.365	.177
Aβ 1-40 (ng/L)	195.946	.267	.793
Aβ42/Aβ40*10	-.061	-.822	.415
T-tau/Aβ42	.161	1.986	.051
P-tau/Aβ42	.022	1.959	.054
ATI	-.326	-2.615	.011
MoCA			
ACE-R			

DISCUSSION

CONCLUSION

Lorem ipsum...

LIMITATIONS

- Sample size:
  - Small sample sizes for both TIA (34) and control (36) groups resulted in statistical variability leading to marginally significant claims
  - Larger sample sizes could reduce the likelihood of Type I and II statistical errors
- Correlation vs. causation:
  - Results concluded that differences exist between TIA patients and healthy controls, but most metrics cannot be attributed to group status

ACKNOWLEDGMENTS

Special thanks to Dr. Beatriz Garcia-Diaz of Webber Academy for guidance throughout the research process.

February 19, 2025

Tasks To-do

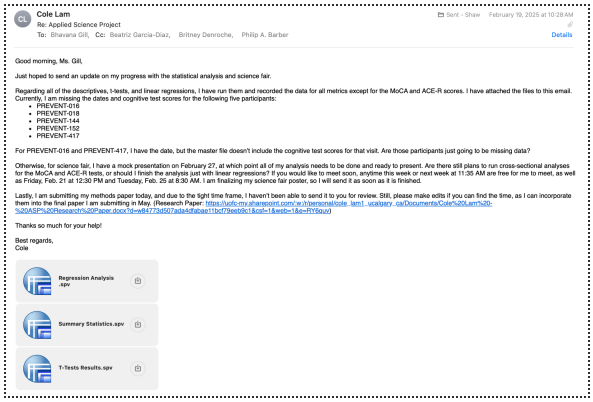
- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Complete Science Fair Poster and Presentation

Tasks Completed

- [x] Research Paper Methodology due Feb. 19

Review

During class, Dr. Garcia reiterated the importance of staying on task and focusing on the science fair. She decided to push the results paper from March 21st to April 14th, but mentioned that the paper should be the easiest section to write because we don't have to explain the data. In fact, for the science fair, we cannot include the "Why" as part of the results. Then, she talked about adding figures and tables, and that the title goes at the bottom for most styles, which need to be followed by a description. Afterward, I made finishing edits to my methods paper, mostly checking for grammar, and then submitted it to GC and Turnitin. Then, I had a biweekly meeting with Dr. Garcia, talking about science fair and my poster, as well as the plans moving forward with whether or not I should try and complete another statistical analysis for science fair. Lastly, I also sent a summary email to my mentors, providing them with the participants whose data I was missing, as well as the remaining time frame and tasks I needed to complete to move forward.



Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber

Sent - Shaw February 19, 2025 at 10:28 AM
Details

Good morning, Ms. Gill,

Just hoped to send an update on my progress with the statistical analysis and science fair.

Regarding all of the descriptives, t-tests, and linear regressions, I have run them and recorded the data for all metrics except for the MoCA and ACE-R scores. I have attached the files to this email. Currently, I am missing the dates and cognitive test scores for the following five participants:

- PREVENT-016
- PREVENT-018
- PREVENT-144
- PREVENT-152
- PREVENT-417

For PREVENT-016 and PREVENT-417, I have the date, but the master file doesn't include the cognitive test scores for that visit. Are those participants just going to be missing data?

Otherwise, for science fair, I have a mock presentation on February 27, at which point all of my analysis needs to be done and ready to present. Are there still plans to run cross-sectional analyses for the MoCA and ACE-R tests, or should I finish the analysis just with linear regressions? If you would like to meet soon, anytime this week or next week at 11:35 AM are free for me to meet, as well as Friday, Feb. 21 at 12:30 PM and Tuesday, Feb. 25 at 8:30 AM. I am finalizing my science fair poster, so I will send it as soon as it is finished.

Lastly, I am submitting my methods paper today, and due to the tight time frame, I haven't been able to send it to you for review. Still, please make edits if you can find the time, as I can incorporate them into the final paper I am submitting in May. (Research Paper: https://ualtc-my.sharepoint.com/:w:/r/personal/cole_lam1_ucalgary_ca/Documents/Cole%20Lam%20-%20ASP%20Research%20Paper.docx?d=w847733d507ada4dfabaa11bcf79eebb9c1&csf=1&web=1&e=RY6guu)

Thanks so much for your help!

Best regards,
Cole

Regression Analysis .spv
Summary Statistics.spv
T-Tests Results.spv

Notes

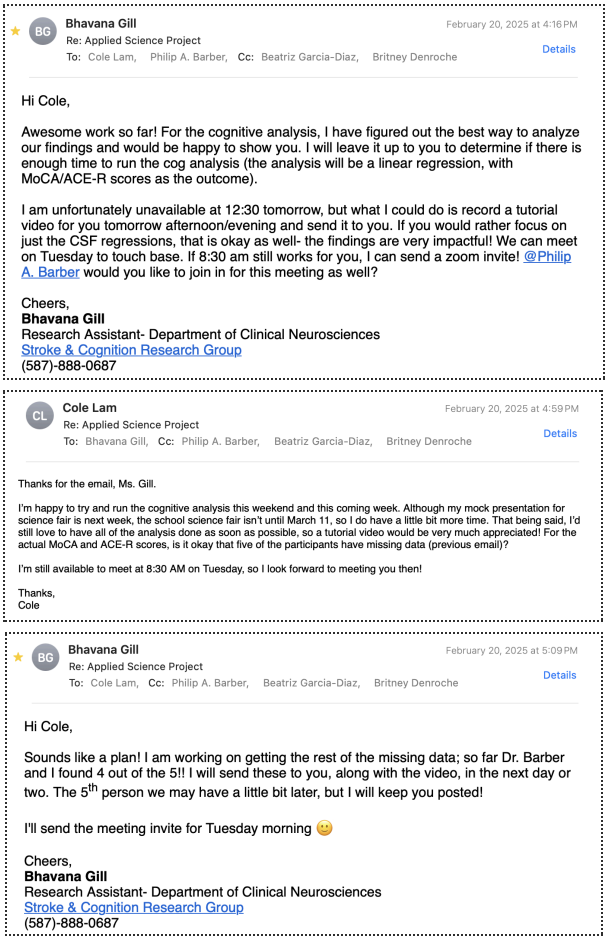
None

February 20, 2025

Tasks To-do	Tasks Completed	Notes
☐ Run descriptive statistics for all demographics, CSF and cognitive data ☐ Run t-tests for all cognitive/CSF data comparing TIAs and controls ☐ Complete Science Fair Poster and Presentation	None	None

Review

This evening, Bhavana and I kept in contact updating the plans moving forward. I communicated that I would like to try and do the extra analysis to even further the nuance of my project, and that I probably would have the time to do, given the school science fair wasn't until Mar. 11, and the CYSF until mid-April. We also confirmed our next meeting for Tuesday, Feb. 25 at 8:30 AM.



Bhavana Gill February 20, 2025 at 4:16 PM
Re: Applied Science Project
To: Cole Lam, Philip A. Barber, Cc: Beatriz Garcia-Diaz, Britney Denroche
Details

Hi Cole,

Awesome work so far! For the cognitive analysis, I have figured out the best way to analyze our findings and would be happy to show you. I will leave it up to you to determine if there is enough time to run the cog analysis (the analysis will be a linear regression, with MoCA/ACE-R scores as the outcome).

I am unfortunately unavailable at 12:30 tomorrow, but what I could do is record a tutorial video for you tomorrow afternoon/evening and send it to you. If you would rather focus on just the CSF regressions, that is okay as well- the findings are very impactful! We can meet on Tuesday to touch base. If 8:30 am still works for you, I can send a zoom invite! @Philip A. Barber would you like to join in for this meeting as well?

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam February 20, 2025 at 4:59 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Philip A. Barber, Beatriz Garcia-Diaz, Britney Denroche
Details

Thanks for the email, Ms. Gill.

I'm happy to try and run the cognitive analysis this weekend and this coming week. Although my mock presentation for science fair is next week, the school science fair isn't until March 11, so I do have a little bit more time. That being said, I'd still love to have all of the analysis done as soon as possible, so a tutorial video would be very much appreciated! For the actual MoCA and ACE-R scores, is it okay that five of the participants have missing data (previous email)?

I'm still available to meet at 8:30 AM on Tuesday, so I look forward to meeting you then!

Thanks,
Cole

Bhavana Gill February 20, 2025 at 5:09 PM
Re: Applied Science Project
To: Cole Lam, Cc: Philip A. Barber, Beatriz Garcia-Diaz, Britney Denroche
Details

Hi Cole,

Sounds like a plan! I am working on getting the rest of the missing data; so far Dr. Barber and I found 4 out of the 5!! I will send these to you, along with the video, in the next day or two. The 5th person we may have a little bit later, but I will keep you posted!

I'll send the meeting invite for Tuesday morning 🙂

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

That evening, I also spent some more time working with my poster and science fair presentation. With the intent of adding more graphics to the poster in place of more words, I replaced the descriptive tables with box and whisker plots, representing the CSF proteins, their ratios, and the cognitive test scores comparing TIA patients with healthy controls.

February 22, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Complete Science Fair Poster and Presentation

Tasks Completed

None

Review

This afternoon, I worked to complete my science fair poster, statistical analyses, and presentations. I started by rerunning all of the statistical analyses to ensure that I didn't make any errors, and converted them into box-and-whisker plots, making aesthetic modifications to make it match my poster. After that, I uploaded all of the statistics onto the poster again, verifying for accuracing and resizing according to what would maximize space. I also ran all of the statistics for the cognitive data even though it was missing to help figure out what the results would generally conclude. I also then wrote up the discussion and conclusion sections for the poster, and added references which I had forgotten to include the first time. I then practiced my speech a few times, trying to figure out where to cut time, given I was over 20 minutes including all of the important details.

Notes

None

February 23, 2025

Tasks To-do

- [ ] Run descriptive statistics for all demographics, CSF and cognitive data
- [ ] Run t-tests for all cognitive/CSF data comparing TIAs and controls
- [ ] Complete Science Fair Poster and Presentation

Tasks Completed

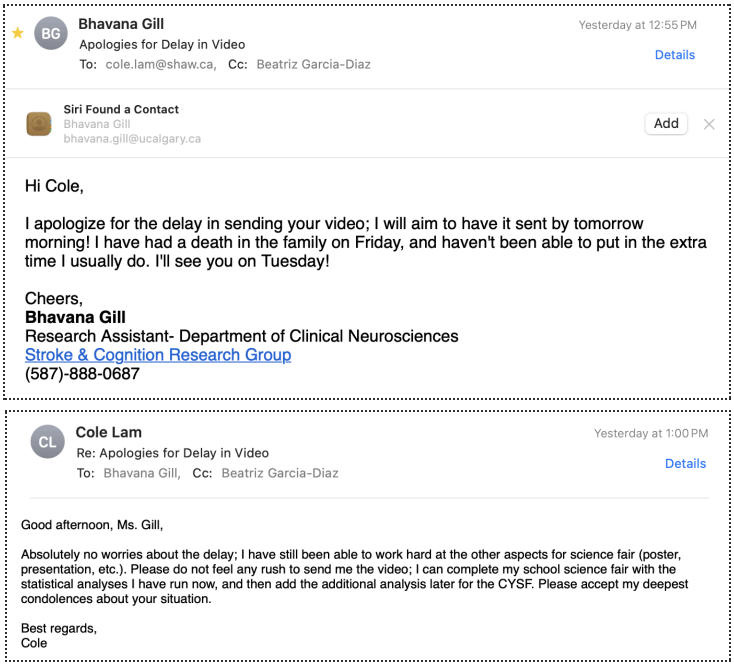
None

Notes

None

Review

Bhavana provided an update on getting all of the cognitive data, explaining there were some delays. I responded by mentioning that I had made enough progress for everything else, particularly for the science fair. Otherwise, I continued to rehearse my science fair presentation, cutting down the time by eliminating less important information.



Bhavana Gill Yesterday at 12:55 PM
Apologies for Delay in Video
To: cole.lam@shaw.ca, Cc: Beatriz Garcia-Diaz
Details

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

I apologize for the delay in sending your video; I will aim to have it sent by tomorrow morning! I have had a death in the family on Friday, and haven't been able to put in the extra time I usually do. I'll see you on Tuesday!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam Yesterday at 1:00 PM
Re: Apologies for Delay in Video
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz
Details

Good afternoon, Ms. Gill,

Absolutely no worries about the delay; I have still been able to work hard at the other aspects for science fair (poster, presentation, etc.). Please do not feel any rush to send me the video; I can complete my school science fair with the statistical analyses I have run now, and then add the additional analysis later for the CYSF. Please accept my deepest condolences about your situation.

Best regards,
Cole

February 24, 2025

Tasks To-do	Tasks Completed	Notes
☐ Complete Science Fair Poster and Presentation	☑ Run descriptive statistics for all demographics, CSF and cognitive data ☑ Run t-tests for all cognitive/CSF data comparing TIAs and controls	None

Review

Over the lunch hour, I met with Dr. Garcia to present my class mock science fair presentation to ask for some improvements and ways that I can remove time. I presented using my poster, in which Dr. Garcia mentioned that it would be more beneficial to use a slideshow with close-up images for the class presentation, given the poster from a far would be illegible and unclear. Other edits involved spending less time explaining my statistical analyses if I was going to go over them later, explaining more the four proteins analyzed in the CSF samples and their relevance in predicting AD pathology, and making everything seem less rehearsed.

Bhavana, in the afternoon, also sent me some of the missing cognitive test scores which I could use to run my analysis. I added them to my SPSS file, and reran the cognitive test statistics (descriptives, t-tests, regressions), added them to my files summarizing the statistics, and updated the poster. Then, Bhavana sent another email seeing if I had other available times to meet, hopefully also with Dr. Barber. I responded saying that Tuesday or Wednesday over the lunch hour (11:35 AM) would be okay to meet.

Bhavana Gill 2:35 PM
Re: Apologies for Delay in Video
To: Cole Lam

Siri Found a Contact
Bhavana Gill
bhavana.gill@ucalgary.ca
Add

Hi Cole,

Thank you for your understanding! I have attached the updated cognitive scores which includes 4/5 participants who were missing..

I may be able to get participant 417's baseline MoCA but this will be likely in the next week or two as it will come in a data transfer from another lab.

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam 2:38 PM
Re: Apologies for Delay in Video
To: Bhavana Gill

Thanks, Ms. Gill,

I'll run all of the cognitive descriptives, t-tests, and regressions without that missing piece of data. Look forward to meeting tomorrow!

Best regards,
Cole

Bhavana Gill 3:46 PM
Meeting availability
To: cole.lam@shaw.ca, Cc: Philip A. Barber
Details

Hi Cole,

I was wondering what your availability looks like for this week? Dr. Barber is unavailable for 8:30 am but maybe we could do another meeting at a time all three of us are available. I am pretty flexible tomorrow, Wednesday, and Thursday!

Cheers,
Bhavana

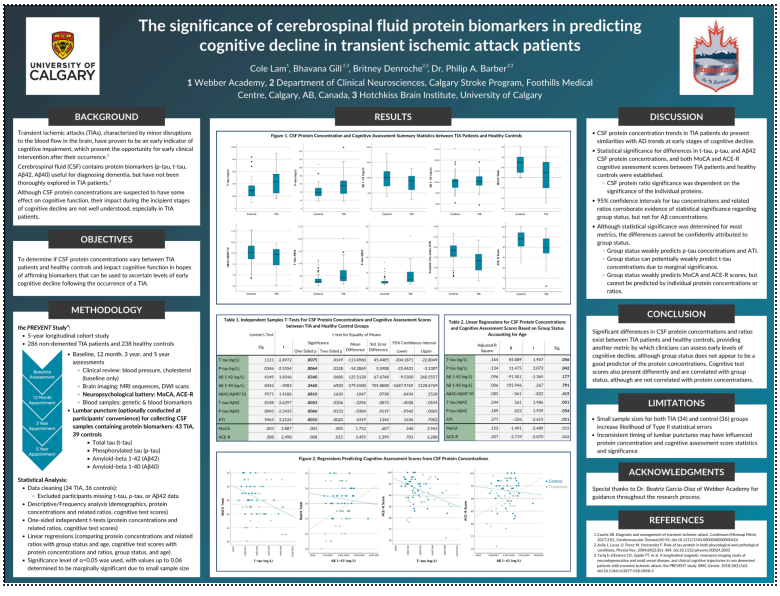
Cole Lam 5:11 PM
Re: Meeting availability
To: Bhavana Gill, Cc: Philip A. Barber
Details

Good evening, Ms. Gill,

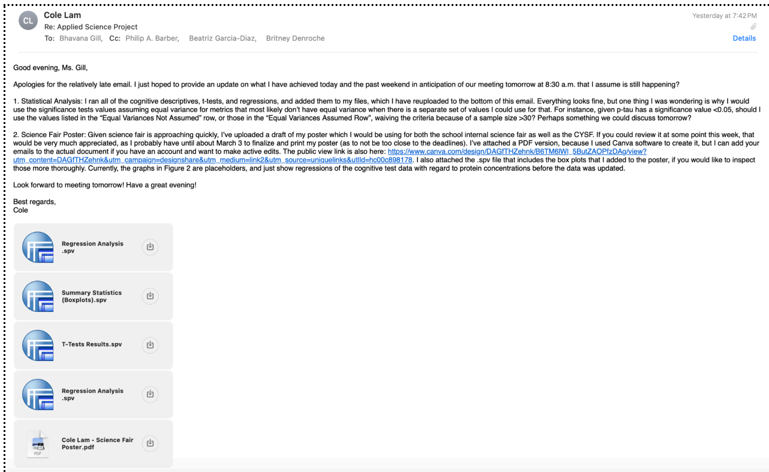
Sorry for the delayed response! Other than tomorrow at 8:30 a.m., **11:35 a.m. tomorrow, or Wednesday also work**. Although I have class on Thursday, that is the day of my science fair presentation, and I also have an appointment over lunch. Hopefully, one of those two times is suitable?

Best regards,
Cole

This evening, I made many of the finishing edits for the science fair based on the updated cognitive data and improvements that Dr. Garcia shared today. For poster edits, for instance, I removed redundant and confusing graph axis labels and filled in some of the underscores for which I didn't have information at the time.



Lastly, this evening, I sent one more summary email, including all of my updated statistics, my science fair poster, and timelines and plans moving forward. I also provided the update that I have my wisdom teeth removal procedure this Friday, so that would also limit my ability to do work this weekend.



Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Cc: Philip A. Barber, Beatriz Garcia-Diaz, Britney Denroche
Yesterday at 7:42 PM
Details

Good evening, Ms. Gill,

Apologies for the relatively late email. I just hoped to provide an update on what I have achieved today and the past weekend in anticipation of our meeting tomorrow at 8:30 a.m. that I assume is still happening?

1. Statistical Analysis: I ran all of the cognitive descriptives, t-tests, and regressions, and added them to my files, which I have reuploaded to the bottom of this email. Everything looks fine, but one thing I was wondering is why I would use the significance tests values assuming equal variance for metrics that most likely don't have equal variance when there is a separate set of values I could use for that. For instance, given p-tau has a significance value <0.05, should I use the values listed in the "Equal Variances Not Assumed" row, or those in the "Equal Variances Assumed Row", waiving the criteria because of a sample size >30? Perhaps something we could discuss tomorrow?

2. Science Fair Poster: Given science fair is approaching quickly, I've uploaded a draft of my poster which I would be using for both the school internal science fair as well as the CYSF. If you could review it at some point this week, that would be very much appreciated, as I probably have until about March 3 to finalize and print my poster (as to not be too close to the deadlines). I've attached a PDF version, because I used Canva software to create it, but I can add your emails to the actual document if you have an account and want to make active edits. The public view link is also here: https://www.canva.com/design/DAGfTHZehnk/B6TM6lWI_5ButZAOPfzDAg/view?utm_content=DAGfTHZehnk&utm_campaign=designshare&utm_medium=link2&utm_source=uniquelinks&utlId=hc00c898178. I also attached the .spv file that includes the box plots that I added to the poster, if you would like to inspect those more thoroughly. Currently, the graphs in Figure 2 are placeholders, and just show regressions of the cognitive test data with regard to protein concentrations before the data was updated.

Look forward to meeting tomorrow! Have a great evening!

Best regards,
Cole

Regression Analysis .spv
Summary Statistics (Boxplots).spv
T-Tests Results.spv
Regression Analysis .spv
Cole Lam - Science Fair Poster.pdf

February 24, 2025

Tasks To-do	Tasks Completed	Notes
☐ Complete Science Fair Poster and Presentation	None	None

Review

This morning, I had my meeting with Bhavana, which was very brief. She mentioned that the linear regressions that would be conducted would have the cognitive tests (MoCA and ACE-R) as the outcomes, and group status, CSF protein concentrations, and age as the predictors. I also asked her about the reasoning for using equal variances assumed values in the independent t-tests would be to allow for the study to have more power to mitigate the risk of Type II errors. Then, when I went back to class, I listened to some oral presentations of other students.

Antara's Science Fair Presentation Notes:

- Background: we are moving towards clean energy (trying to limit greenhouse gas emissions)
  - PEMFCs work by separating electrons and protons in the anode and combining with oxygen
    - Catalyst ink facilitates the reactions and is most important
- Research Question:
  - How do catalyst ink parameters affect the performance of a PEMFC?
- Hypothesis: more alcohol will improve catalyst layer coverage and facilitate more efficient processes
- Methods:
  - Catalyst ink was prepared
  - Average particle size, electrical conductivity, and average pore width were then determined
- Results:
  - Compares water content to all the metrics
    - Nonlinear trends because of complex interactions
- Conclusions:

        - 15% water content appears to be most suitable across all metrics
        - Higher conductivity and decreased resistance → more efficient
            - Particle size should be lower
            - Pore width needs to be "optimal" (often larger) (25% seems to be best for this)

Nina's Science Fair Presentation Notes:

- Background: Alcohol use disorder (AUD) is prevalent worldwide. It's also hard to treat because it affects people differently.
    - Psilocybin has been found to potentially help with this, but has not been thoroughly explored.
    - Classical Psychedelics: psilocybin, affects serotonin receptors
- Research Question: how are motivations and expectations when participating in psilocybin treatment affect the outcome.
- Hypothesis: more positive expectation/degree of motivation → experience greater reduction in alcohol consumption
- Variables:
    - Independent: patients motivations
    - Dependent: changes in alcohol consumption
- Objectives: collect data on motivations/expectations; monitor trends in patients' changes in alcohol consumptions; fill in the current knowledge gap; provide framework for personalizing psilocybin therapy
- Significance: reduce stigmas around AUD; enhance effectiveness of psilocybin-assisted therapy; maximize positive outcomes
- Methods:
    - Screening Visit→ baseline visit→prep visit→dosing visit→1 day meeting→2 week meeting→3 week meeting→4 week meeting→12 week meeting
    - Screening for methodology involved largely free-response questions to limit response/non-response bias
- Analysis:
    - Results are currently weak due to a small sample size
- Future steps:
    - Collect more data
    - Help design more effective intervention development

Eleanor's Science Fair Presentation Notes:

- Background: climate has been a significant factor in influencing human societies
    - Technological advancements have helped reduce the negative impact of natural disaster
    - El Niño: a phase of El Niño Southern Oscillation (ENSO) that causes differences in temperature
        - Impacts fisheries, health, population, agriculture, etc. in Peru and India
    - Analyzed Peru and India
        - Peru because it is very significantly impacted by El Niño
        - India because El Niño did have a very significant impact for that same time period
    - Restriction: old data from a long time ago is really hard to procure:
        - Solution: proxy records of ice cores and tree rings can be used to predict the impact of El Niño during those times
    - From 1788-1793 to 1982-1983, we see changes in climate change and economic development
- Question: What were the agriculture, economic, and demographic impacts of the El Niño events comparing the two time periods (listed above)?
    - Sub Question: is modern society more resilient to changes in climate change, and can it be used to predict future occurrences?
- Significance: there has been a doubling in the occurrences of more severe natural disasters and significant climate changes
- Methods:
    - Reconstructing ENSO from 1700 to present:
        - Collated proxy records from previous studies
        - Raw data was gathered and reorganized
        - Correlations where established
        - Scatter Plots and regressions were constructed using the data
    - Measuring regional impacts:

        - Looked at economic and agriculture fishery data, as well as other regional data
- Results:
    - There are consistent results and similar amplitudes for the El Niño events across the two time periods.
    - Impacts in the 18th century in India: food prices spiked and resulted in much death
    - Impacts in the 20th century in India: no significant population loss resulting from the event, but there was a halt in the increase of grain production
    - Impacts in the 18th century in Peru: there was a crisis in fisheries and crop failure
    - Impacts in the 20th century in Peru: fishery growth decreased by 270%; significant decrease in Peru's GDP
- Analysis:
    - Both time periods experienced some loss, but it was much more controlled and remediable in the 20th century.
    - Agriculture still remains dependent on stable weather, but better with technological advancements
- Future Directions:
    - Access to more data would be great
    - Expanding the region of study to more developed countries as well
    -

February 25, 2025

Tasks To-do	Tasks Completed	Notes
☐ Complete Science Fair Poster and Presentation	None	None

Review

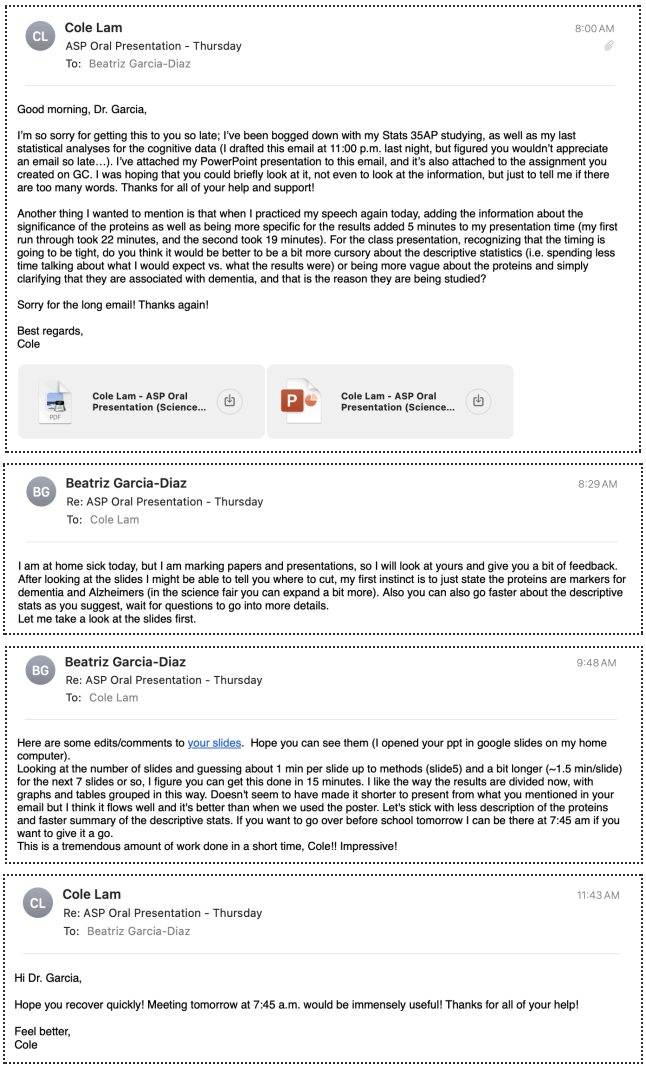
This evening, I worked late to transcribe my poster into a powerpoint presentation to allow for a better class presentation. I practiced my oral presentation again, using Dr. Garcia's revisions, which ended up being 20 minutes (too long again…). It was most likely because I spent lots of time talking about the results, intentionally being somewhat repetitive about the statistical significance of certain values. Consequently, even though I only spent 5-6 minutes on going through the background, objectives, and methods, it would still take me 15 minutes to cover the rest of the content, largely due to the number of statistical analyses conducted. To gain another perspective, I then drafted an email to send to Dr. Garcia to see if she could review my powerpoint briefly to let me know if there were too many words. But because it was late (11:00 PM), I schedule it to send the next morning at 8:00 AM.

February 26, 2025

Tasks To-do	Tasks Completed	Notes
☐ Complete Science Fair Poster and Presentation	None	None

Review

This morning, Dr. Garcia emailed me back after my scheduled email was sent, providing some edits and offering to meet with me Thursday morning to let me present one more time. This evening, I made her revisions to my powerpoint presentation and practiced my oral presentation two more times.



Cole Lam 8:00 AM
ASP Oral Presentation - Thursday
To: Beatriz Garcia-Diaz

Good morning, Dr. Garcia,

I'm so sorry for getting this to you so late; I've been bogged down with my Stats 35AP studying, as well as my last statistical analyses for the cognitive data (I drafted this email at 11:00 p.m. last night, but figured you wouldn't appreciate an email so late…). I've attached my PowerPoint presentation to this email, and it's also attached to the assignment you created on GC. I was hoping that you could briefly look at it, not even to look at the information, but just to tell me if there are too many words. Thanks for all of your help and support!

Another thing I wanted to mention is that when I practiced my speech again today, adding the information about the significance of the proteins as well as being more specific for the results added 5 minutes to my presentation time (my first run through took 22 minutes, and the second took 19 minutes). For the class presentation, recognizing that the timing is going to be tight, do you think it would be better to be a bit more cursory about the descriptive statistics (i.e. spending less time talking about what I would expect vs. what the results were) or being more vague about the proteins and simply clarifying that they are associated with dementia, and that is the reason they are being studied?

Sorry for the long email! Thanks again!

Best regards,
Cole

Cole Lam - ASP Oral Presentation (Science... | Cole Lam - ASP Oral Presentation (Science...

Beatriz Garcia-Diaz 8:29 AM
Re: ASP Oral Presentation - Thursday
To: Cole Lam

I am at home sick today, but I am marking papers and presentations, so I will look at yours and give you a bit of feedback. After looking at the slides I might be able to tell you where to cut, my first instinct is to just state the proteins are markers for dementia and Alzheimers (in the science fair you can expand a bit more). Also you can also go faster about the descriptive stats as you suggest, wait for questions to go into more details.
Let me take a look at the slides first.

Beatriz Garcia-Diaz 9:48 AM
Re: ASP Oral Presentation - Thursday
To: Cole Lam

Here are some edits/comments to your slides. Hope you can see them (I opened your ppt in google slides on my home computer).
Looking at the number of slides and guessing about 1 min per slide up to methods (slide5) and a bit longer (~1.5 min/slide) for the next 7 slides or so, I figure you can get this done in 15 minutes. I like the way the results are divided now, with graphs and tables grouped in this way. Doesn't seem to have made it shorter to present from what you mentioned in your email but I think it flows well and it's better than when we used the poster. Let's stick with less description of the proteins and faster summary of the descriptive stats. If you want to go over before school tomorrow I can be there at 7:45 am if you want to give it a go.
This is a tremendous amount of work done in a short time, Cole!! Impressive!

Cole Lam 11:43 AM
Re: ASP Oral Presentation - Thursday
To: Beatriz Garcia-Diaz

Hi Dr. Garcia,

Hope you recover quickly! Meeting tomorrow at 7:45 a.m. would be immensely useful! Thanks for all of your help!

Feel better,
Cole

February 27, 2025

Tasks To-do	Tasks Completed	Notes
None	☑ Complete Science Fair Poster and Presentation	None

Review

This morning, I met with Dr. Garcia at 7:45 AM to run through my presentation one more time. It ended up being about 18 minutes (a bit long), but she helped me establish what was good (background and methods) and what could be shortened (some results and statistical analyses). Then in class, I presented first, which ended up being quite a bit longer than I had hoped… After that, I listened to others' presentations.

Amber's Science Fair Presentation Notes:

- Background: Anesthetics are useful for inducing unconsciousness and reducing pain for surgeries
    - Specific type: sevoflurane
        - More immediate effects
    - Synapses: important for neurons to interact
    - Relationship between sevoflurane and synapses:
        - The anesthetics blocks the receptors which stops pain electrical signals
    - Problem: anesthetics may cause permanent reduction in electrical signals of synapses
    - Synaptophysin and PSD-95 are specific proteins relevant and are impacted by anesthetics
- Research question: How does repeated sevoflurane exposure affect synapse formation?
    - Changes in formation
    - Changes in density
    - Changes in proteins
- Methods:
    - Hippocampus in rats is isolated, and the cells are dissociation (rat brains are similar to humans)
    - Then, the cells were plated and grown
    - After 7 days of growing, synaptic activity was monitored to ensure synapses were forming
    - Half the samples were exposed to sevoflurane
    - Then, the cells were stopped and preserved
    - Then staining was used and then they were imaged
- Results:
    - PSD-95 and synaptophysin were assessed with different colours
    - Neurons were significantly synaptically less dense in the sevoflurane group
- Significance:
    - Helps better understand the impact of anesthetics on synapse density
    - It is assumed that even one exposure would have an impact, but it would be less severe than what was shown in the experiment. **Repeated exposure is the real problem**.

Audrey's Science Fair Presentation Notes:

- Significance: There are many E. coli O157 cases every year, and E. coli O157 is antibiotic resistance, but bacteriophages might be the solution
    - Provides the basis for better understanding on how E. coli O157 interacts with bacteriophages
    - Biological systems would be a next step
- Background:
    - Genetic components: antiviral defense systems, single-nucleotide polymorphisms
- Topic: exploring the role of bacteriophages and their potential to deal with E. coli O157
- Methods:
    - Phage Exposure → DNA Extraction → WGS → Analysis →Visualization
- Results:
    - Defense System vs. Isolates: isolates didn't change much with bacteriophage exposure

    - Genetic similarity map: many isolates were very similar, and that mutation didn't really occur
        - Even mutations that occurred were still very similar
    - More heatmaps: show similarities between certain isolates with regard to single-nucleotide polymorphisms

Marie-Elise's Science Fair Presentation Notes:

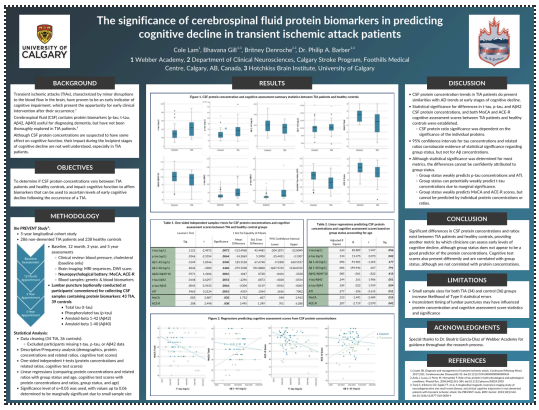
- Significance/Objectives: how can user accessibility in technology/applications be improved for people around the world, based on age, disabilities, and other metrics.
- Limitations:
    - Speech, Reading, Writing, Movement, etc. are not studied and could be covariates
- Methods:
    - She created a website that had a Connect 4 game and checkers game, which has speech recognition.
    - Ethics forms and surveys are also included.
- Variables:
    - Manipulated: modes of control, limitations/age
    - Response: preferred mode of interaction
    - Controlled: type of games, complexity, etc.
    - Confounding: sex, preferences, etc.
- Research Question: how do people's preferences and age influence their preferred mode of playing the game
- Hypothesis: there is a difference in the preferred mode of playing between the elderly and young individuals
- Results:
    - Anxiety is the most identified condition from the survey
    - 61% preferred speech recognition, vs. 39% for gesture tracking
        - Increasing age, greater preference to speech recognition
        - Pretty high R squared values (~0.7)
    - People with anxiety, ADHD, difficulty speaking/reading, etc. prefer gesture tracking
    - Grouped conditions were also analyzed (anxiety → gesture tracking)
        - Anxiety itself had that trend, but it also impacted the other conditions if they have it.
- Conclusions:
    - People that prefer gesture recognition had ADHD, anxiety, difficulty reading/writing
    - Everyone else preferred speech (61%)
    - Age: older individuals preferred speech, and younger individuals preferred gesture tracking
- Project improvements:
    - This study was the first step in better understanding preferences based on certain conditions
    - A larger sample size is always better (even though relatively high R squared value)
    - Technology should adapt to what people want (adaptive AI?)

Lauren's Science Fair Presentation Notes:

- Background: lung cancer fatalities are high
    - Current treatment methods are dangerous and sometimes not fully successful
    - But lifestyle changes and other interventions may provide a less uncomfortable treatment.
    - Looking at Stage IIIB/C non-small cell lung cancer (NSCLC)
        - Looking specifically at adenocarcinomas and squamous cell carcinomas
    - Current standard for treatment:
        - First, tumours are surgically removed
        - Then, targeted cancer medication or chemoradiation therapy
        - Lastly, intervention and immunotherapy
            - Interventions are optional but becoming more standard
    - What are interventions:
        - Aims to reduce treatment toxicity and improve patient survival via changes to lifestyle and medications
- Significance:
    - Lung cancer is one of the most fatal cancers.

    - Many people cannot complete full treatments due to toxicity and discomfort
- Research Question: what are potential interventions that are not commonly used right now to improve the prognosis of NSCLC?
- Methods:
    - Papers were pulled from databases, sorted, and then determined if it met the exclusion criteria.
        - Exclusion criteria: no systematic reviews or published prior to 2009
    - Papers were then sorted into the intervention type (many were meta-analyses)
        - So, references were used to pull the original research
    - Then, treatments were scored
        - Efficacy (0-5)
        - Cost effectiveness (1-5)
        - Feasibility (1-5)
        - Intervention types:
            - Dietary (caloric intake, fatty acid supplements)
            - Activity (exercise, breathing exercises, etc.)
- Results:
    - Many papers were traditional chinese medicines (TCMs) that are so diverse and not widely accessible.
        - Therefore, these were not analyzed.
    - Others were diet, activity, and medication.
        - Medications were not the most useful because they don't have a uniformity and may be part of the treatment (not intervention).
    - Tables:
        - Exercise: 14, 14, 14.5
            - Seems to be the best intervention right now
        - Breathing Exercise: 14
        - Diet: 9, 13, 13
            - Often supplements are expensive
- Sources of Error:
    - Small database after the application of exclusion criteria
        - Allowed very precise conclusion, but unfortunately based on very little research
    - Lack of uniformity across studies made comparisons more difficult
- Future directions/significance:
    - Larger database would be better to mitigate possible error
    - Greater focus on certain outcomes (toxicity, quality of life)
    - Other directions

This evening, I also spent some time looking at my science fair poster again. I hoped to revise some of the naming and capitalization for terms like *t* test and t-tau, which shouldn't be capitalized, and therefore, should not be at the beginning of a sentence.



Daily Notes

March 3, 2025

Tasks To-do

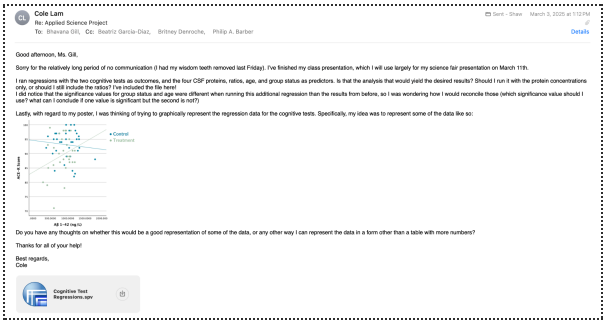
- [ ] Finalize poster and presentation for science fair (New)

Tasks Completed

None

Review

This day, after my wisdom teeth extraction the previous Friday, I conducted the last of my statistical analyses, running the regressions with the cognitive test as outcomes and the different CSF proteins and their respective concentrations as predictors, along with age and group status. I then sent an email to Bhavana and Dr. Barber mentioning that my class oral presentations were finalized, but that the Webber internal science fair was soon. I uploaded my finished stats analysis, asking to confirm that it was executed properly, and also asked a few questions (1. Why were the *t* tests run assuming equal variance when they weren't, especially given that the output included values for equal variances not assumed?; 2. Are graphical representations of regressions a good way to express the strength of the regressions, or are the tables with the P values integral for illustrating any significance?)


Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Dennoche, Phillip A. Barber

Good afternoon, Ms. Gill,

Sorry for the relatively long period of no communication (I had my wisdom teeth removed last Friday). I've finished my class presentation, which I will use largely for my science fair presentation on March 11th.

I ran regressions with the two cognitive tests as outcomes, and the four CSF proteins, ratios, age, and group status as predictors. Is that the analysis that would yield the desired results? Should I run it with the protein concentrations only, or should I still include the ratios? I've included the file here!
I did notice that the significance values for group status and age were different when running this additional regression than the results from before, so I was wondering how I would reconcile those (which significance value should I use? what can I conclude if one value is significant but the second is not?)

Lastly, with regard to my poster, I was thinking of trying to graphically represent the regression data for the cognitive tests. Specifically, my idea was to represent some of the data like so:

Control
Treatment

Do you have any thoughts on whether this would be a good representation of some of the data, or any other way I can represent the data in a form other than a table with more numbers?

Thanks for all of your help!

Best regards,
Cole

Cognitive Test Regressions.xlsx

Lastly, I made minor edits to my poster by finding better Webber Academy and the University of Calgary logos, while also increasing the font size on the tables to improve visibility.

Notes

None

March 4, 2025

Tasks To-do	Tasks Completed	Notes
☐ Finalize poster and presentation for science fair	None	None

Review

This morning, realizing the urgency of the situation (needing to print the poster ASAP given that it takes several business days to actually print), I sent emails to Bhavana and Dr. Garcia to see if they could review my poster briefly so I could send it in for printing. Bhavana helped me revise my statistical analyses a little bit, and provided some poster feedback that I would employ (i.e. adding the linear regressions as tables).

Cole Lam
Re: Applied Science Project
To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Britney Denroche, Philip A. Barber

Sent - Shaw March 4, 2025 at 8:03 AM

Details

Good morning, Ms. Gill,

I've been finalizing my science fair presentation, and recognizing that I need to print my poster very soon, I'd like to run the content, organization, and design by you one last time. Using my "weird" regression analysis that I sent yesterday, I added some figures that show that the association between protein concentrations and ratios is not particularly valuable. I hope to send my poster for printing even tonight or tomorrow evening, so if you could review it briefly sometime soon, your help would be greatly appreciated. Here is the public view link (I've also attached a PDF below):
https://www.canva.com/design/DAGITHZehnk/B6TM6IWl_9BuiZAOPtsDAg/view?utm_content=DAGITHZehnk&utm_campaign=designshare&utm_medium=link2&utm_source=uniquelinks&utlId=h0008981178

Thanks for immense help and guidance!

Best regards,
Cole

Cole Lam
Re: Applied Science Project
To: Beatriz Garcia-Diaz

Sent - Shaw March 4, 2025 at 8:03 AM

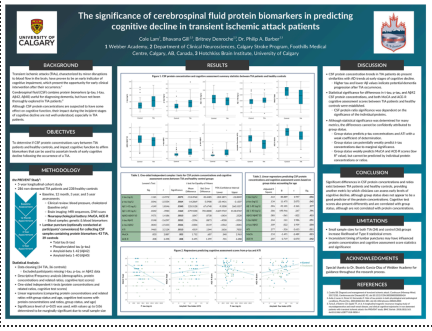
Good morning, Dr. Garcia,

I'm not sure whether I properly strung these scheduled emails... but would you mind reviewing my poster briefly sometime within the next few days? I hope to get it into printing Thursday at the latest, and I should have had an email sent to Bhavana at 8:00 AM this morning as well. I finalized all the changes, and plan on printing out this poster on a 36" tall and 48" wide foam poster board, and propping it up with a canvas stand on the table. Please let me know what you think!

(In case you can't access the updated poster from the other scheduled to send at 8:00 AM, I reattached the links/files here: https://www.canva.com/design/DAGITHZehnk/B6TM6IWl_9BuiZAOPtsDAg/view?utm_content=DAGITHZehnk&utm_campaign=designshare&utm_medium=link2&utm_source=uniquelinks&utlId=h0008981178)

I'm so so sorry for sending this behind schedule!

Best regards,
Cole



Bhavana Gill — March 4, 2025 at 10:59 AM

Re: Applied Science Project

To: Cole Lam

Hi Cole!

Did you get the video I sent regarding the regressions? Just to clarify, the predictors of each cognitive model should be: one of the proteins & age. You would repeat this for each protein & protein ratio for both the MoCA and ACE-R. Does that make sense? From here, you would use the values in the row of the proteins (that means the model held age constant).

It would be incorrect to add all the protein and protein ratios into one model.

I'll take a look at the poster this afternoon! I'm so excited for you to share your project!!

Cheers,
Bhavana

Bhavana Gill — March 4, 2025 at 11:00 AM

Re: Applied Science Project

To: Cole Lam

May you also resend the regression SPSS file? It doesn't open for me!!

Cheers,
Bhavana

Cole Lam — March 4, 2025 at 11:12 AM

Re: Applied Science Project

To: Bhavana Gill, Cc: Britney Denroche, Beatriz Garcia-Diaz, Philip A. Barber — Details

Hi Ms. Gill,

I'm not sure I got the video… I was looking back through my emails, but I cannot find it… I'll rerun the statistics quickly (my initial file you cannot open is not right). I'll send you the updated files ASAP (later today)! The graphs representing the regressions should still be valid (they weren't contingent on the regression significance values), but considering that group status is not to be involved in the analysis, should I use a line of best fit representing all of the data and not dividing the data based on group status?

Thanks,
Cole

Cole Lam — Sent - Shaw — March 4, 2025 at 11:35 AM

Re: Applied Science Project

To: Bhavana Gill, Cc: Britney Denroche, Beatriz Garcia-Diaz, Philip A. Barber — Details

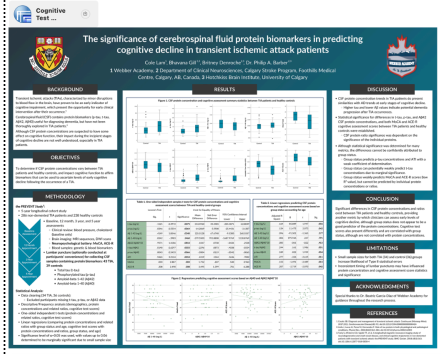
Good morning, Ms. Gill,

I quickly ran the regressions again just now, so hopefully it looks right. It seems that nothing is significant, although Aβ40 had a value of 0.07 only for the MoCA, which I found kind of weird. Was there a problem with the stats that I ran, or are these results just really not significant?

On a separate note, I updated my poster slightly (https://www.canva.com/design/DAGfTHZehnk/B6TM6lWl_5ButZAOPfzDAg/view?utm_content=DAGfTHZehnk&utm_campaign=designshare&utm_medium=link2&utm_source=uniquelinks&utlId=hc00c898178), changing the metrics that I represented and combining the data so that group status was not a marker. Please let me know what you think!

Best regards,
Cole

Cognitive Test ...



Bhavana Gill March 4, 2025 at 12:42 PM
Re: Applied Science Project
To: Cole Lam, Cc: Britney Denroche, Beatriz Garcia-Diaz, Philip A. Barber Details

Hi Cole,

I just re-uploaded the SPSS tutorial video the the folder I shared with you previously! Let me know if you can find it. I also realize I definitely forgot to add in group status as a predictor in the email I sent you this morning. The predictors should be a protein, age, and group status (see video). Re-run these, and let me know what you get.

As for presenting the data- you could use a figure like you showed me before (the scatter plot for the regression data), or you may opt to create a table with the regression values (usually the beta value, and significance value). Personally, I have used box plots to represent the group differences on the protein levels & moca scores, and then a table to display the regression findings.

I'll take a look at your poster now, and will re-look at it once the regressions are updated. Really good job so far!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687

Cole Lam March 4, 2025 at 1:00 PM
Re: Applied Science Project
To: Bhavana Gill, Cc: Britney Denroche, Beatriz Garcia-Diaz, Philip A. Barber Details

Thanks for the re-upload, Ms. Gill,

I can access the video now! (It's weird that I didn't find it there before…) I reran the statistics, and the results were marginally different, and still, none of the proteins revealed significance. Also, the Aβ40 has the most significant value (0.075), which seems odd because it only has that value for the MoCA tests, but a much larger value for the ACE-R test.

Best regards,
Cole

Cognitive Test Regressions.spv

Bhavana Gill Inbox - Shaw March 4, 2025 at 1:04 PM
Re: Applied Science Project
To: Cole Lam, Cc: Beatriz Garcia-Diaz, Philip A. Barber Details

Hi Cole,

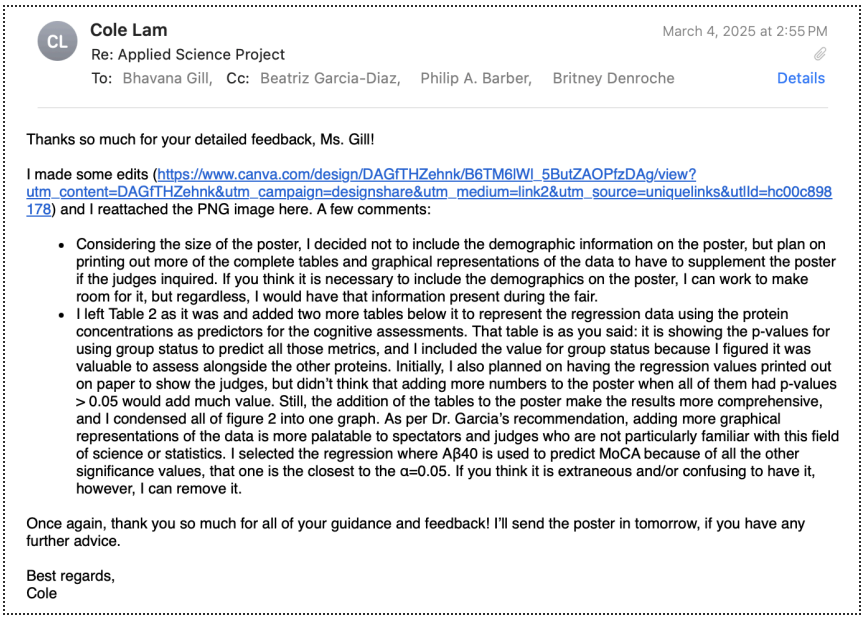
Poster notes:

- Do you need to report demographics? This usually includes age, sex, education, and possibly the mean values of the Moca and Ace-r of both TIAs and controls. I can share a table I made previously if you would like an example.
- Table 2 is a little confusing for me. Specifically, you should have ran 6 models for the MoCA and 6 for the ACE-R, but I only see one row for each cognitive test. I am assuming these are the p-values for group status while holding age constant, but the purpose of running the cognitive regressions was to see if the protein levels could predict cognitive outcomes. I think the video will help explain, but you should be looking at the values reported in the same row as the CSF protein, not the group status row because we are trying to see if Abeta42 (for example) can significantly predict Moca scores regardless of age/group status. I hope this makes since!

This would mean you will likely need another table, or change your figures

- Why did you choose to only display the regressions for AB40 and Ab42/40?
- The first point in the discussion should have a reference.
- I would also include a point about why it is shocking to see differences in tau ... This is because some literature suggests increased tau in CSF is a marker of neurofibrillary tangles in the brain (marker of AD). I can send some references on this if you'd like!

Cheers,
Bhavana Gill
Research Assistant- Department of Clinical Neurosciences
Stroke & Cognition Research Group
(587)-888-0687



Cole Lam March 4, 2025 at 2:55 PM

Re: Applied Science Project

To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Thanks so much for your detailed feedback, Ms. Gill!

I made some edits (https://www.canva.com/design/DAGfTHZehnk/B6TM6lWl_5ButZAOPfzDAg/view?utm_content=DAGfTHZehnk&utm_campaign=designshare&utm_medium=link2&utm_source=uniquelinks&utlId=hc00c898178) and I reattached the PNG image here. A few comments:

- Considering the size of the poster, I decided not to include the demographic information on the poster, but plan on printing out more of the complete tables and graphical representations of the data to have to supplement the poster if the judges inquired. If you think it is necessary to include the demographics on the poster, I can work to make room for it, but regardless, I would have that information present during the fair.
- I left Table 2 as it was and added two more tables below it to represent the regression data using the protein concentrations as predictors for the cognitive assessments. That table is as you said: it is showing the p-values for using group status to predict all those metrics, and I included the value for group status because I figured it was valuable to assess alongside the other proteins. Initially, I also planned on having the regression values printed out on paper to show the judges, but didn't think that adding more numbers to the poster when all of them had p-values > 0.05 would add much value. Still, the addition of the tables to the poster make the results more comprehensive, and I condensed all of figure 2 into one graph. As per Dr. Garcia's recommendation, adding more graphical representations of the data is more palatable to spectators and judges who are not particularly familiar with this field of science or statistics. I selected the regression where Aβ40 is used to predict MoCA because of all the other significance values, that one is the closest to the α=0.05. If you think it is extraneous and/or confusing to have it, however, I can remove it.

Once again, thank you so much for all of your guidance and feedback! I'll send the poster in tomorrow, if you have any further advice.

Best regards,
Cole

March 5, 2025

Tasks To-do

- [ ] Finalize poster and presentation for science fair

Tasks Completed

None

Review

In class, I talked to Dr. Garcia about my final poster edits. I asked her about ways to make the poster more accessible to the layperson, and how to make the text easier to read (considering its preponderance relative to the figures/tables/graphs). She printed off the poster on US letter sized paper, looking at the text size, figure size, and table sizes. Overall, she helped me conclude that the font is large enough that it doesn't become dizzying to read, and the tables especially would be nice and large. She did recommend that I make the background research bullet points to be more clear which points were distinct, and she also helped me make sure my acknowledgements were good. This evening, I sent the poster in for printing on a 48" by 36" foam board. I also ordered a canvas stand off of Amazon to prop the poster up.

Notes

None

March 6, 2025

Tasks To-do

- [ ] Finalize poster and presentation for science fair

Tasks Completed

None

Review

Because I could not put all of my tables and figures onto the poster board (obviously), I started compiling all of the raw tables and graphs into a single document that I planned on printing to accompany the poster. Specifically, there were demographic tables, more complex *t* test and regression tables (accompanied by ANOVA tests), and potential graphical representations of the data that I wanted to still have to show the judges. I also did a little bit of research into the other metrics that were presented in the tables (eg. ANOVA tests, degrees of freedom, unstandardized B values, etc.).

Notes

None

March 7, 2025

Tasks To-do

None

Tasks Completed

- [x] Finalize poster and presentation for science fair

Review

This day, I made finishing edits to my results document that I would print, specifically adding all of the graphical regression representations to the tables (Model Summary, ANOVA, Coefficients). The poster was also picked up, which turned out quite nice (the font size was nice and large).

Notes

None

March 8, 2025

Tasks To-do

None

Tasks Completed

None

Review

This morning, I went out to print my results document, as well as a few supporting documents. Although there were some problems with the printing process, the results document, being over 90 pages long, was successfully printed and bound. I also printed off my background research to show the judges in case they were wondering about the sparseness of background information on the poster, the MoCA and ACE-R assessments that are given to PREVENT participants, and some paper poster copies.

Notes

None

March 10, 2025

Tasks To-do

None

Tasks Completed

None

Review

This evening, I finalized and practiced my science fair presentation, timing myself and recording to listen to and make edits. I collected all of my documents and made sure they were in order, and prepped my laptop for showing the logbook if necessary.

Notes

1. Webber Academy Internal Science Fair is tomorrow!

March 11, 2025

Tasks To-do

None

Tasks Completed

None

Review

Throughout the day, I presented my science fair project to the Webber Academy judges, which included a combination of former Webber alumni and Applied Science Project mentors. Overall, the day went quite well, with a few questions about the conclusions of the data and the small sample size, but not much else. The judges also really liked the printed copies of the posters, so I would make sure to print more to bring to the CYSF.

Notes

1. Webber Academy Internal Science Fair is today!

March 12, 2025

Tasks To-do

- [ ] Complete the CYSF portal (New)

Tasks Completed

None

Review

This afternoon, the award ceremony for the Webber Academy Internal Science Fair was held, in which judges feedback was released, CYSF advancements were announced, along with first, second, and third place projects for junior high and senior high. Wonderfully, I advanced to the CYSF as the top senior high and senior school project, so I would need to finish my CYSF portal as soon as possible.

Notes

None

March 13, 2025

Tasks To-do

- [ ] Complete the CYSF portal

Tasks Completed

None

Review

In class, Dr. Garcia made sure to clearly emphasize the path forward approaching the science fair. Specifically, she noted the importance of getting the CYSF portals done with much care, given that in previous years, the judges for the CYSF had gone onto the portals to carefully understand the project and prepare questions. I went through my portal through the sections that I had already completed (problem, methods, background research) and made final edits to make sure it was focused on my project. Within the background research, there was a section relating to APOE that I considered removing, but decided to keep because it was relevant to my old project which I may end up bringing up, and because it shows I have a holistic understanding of clinical neuroscience broad enough for the scope of my project.

Notes

None

March 16, 2025

Tasks To-do

- [ ] Complete the CYSF portal

Tasks Completed

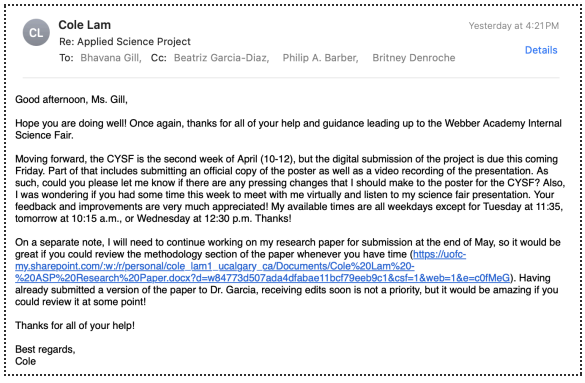
None

Notes

None

Review

This evening, after a late robotics tournament, I sent an email to Bhavana providing an update on the status of the science fair, considering that I would need to submit the portal soon. I asked if I could present the project to her at some point for some edits, and also mentioned that the research paper is the next big assessment that will require some editing.



CL **Cole Lam** Yesterday at 4:21PM

Re: Applied Science Project

To: Bhavana Gill, Cc: Beatriz Garcia-Diaz, Philip A. Barber, Britney Denroche Details

Good afternoon, Ms. Gill,

Hope you are doing well! Once again, thanks for all of your help and guidance leading up to the Webber Academy Internal Science Fair.

Moving forward, the CYSF is the second week of April (10-12), but the digital submission of the project is due this coming Friday. Part of that includes submitting an official copy of the poster as well as a video recording of the presentation. As such, could you please let me know if there are any pressing changes that I should make to the poster for the CYSF? Also, I was wondering if you had some time this week to meet with me virtually and listen to my science fair presentation. Your feedback and improvements are very much appreciated! My available times are all weekdays except for Tuesday at 11:35, tomorrow at 10:15 a.m., or Wednesday at 12:30 p.m. Thanks!

On a separate note, I will need to continue working on my research paper for submission at the end of May, so it would be great if you could review the methodology section of the paper whenever you have time (https://uofc-my.sharepoint.com/:w:/r/personal/cole_lam1_ucalgary_ca/Documents/Cole%20Lam%20-%20ASP%20Research%20Paper.docx?d=w84773d507ada4dfabae11bcf79eeb9c1&csf=1&web=1&e=c0fMeG). Having already submitted a version of the paper to Dr. Garcia, receiving edits soon is not a priority, but it would be amazing if you could review it at some point!

Thanks for all of your help!

Best regards,
Cole

March 17, 2025

Tasks To-do

- [ ] Complete the CYSF portal

Tasks Completed

None

Review

This afternoon and evening, I worked hard to nearly finalize the entire CYSF portal. Notably, I completed the data and conclusions sections, adding the tables and graphs and summarizing the results. I had lots of technical problems trying to add the tables, so I added a comment at the top apologizing for the ambiguity and poor layout of the tables, citing that I attached my results document at the bottom that would allow them to look through the results without worrying about strange formatting. I then drew my conclusions, and added my limitations and project improvements to the conclusion, given there is no official spot for it.

Notes

None

March 18, 2025

Tasks To-do

- [ ] Complete the CYSF portal

Tasks Completed

None

Review

This evening, I planned on recording my presentation for the CYSF portal. I decided to practice with the poster, but my presentation came consistently around 12-13 minutes. Ultimately, I still decided to record to practice, but later decided that it might be better to record the presentation alongside a powerpoint given that it is difficult to see the poster content in the video without zooming in. So, I worked at the presentation, creating a Prezi to have a nice flow of information from one slide to another.

Notes

None

March 19, 2025

Tasks To-do

None

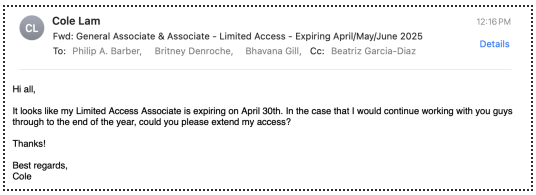
Tasks Completed

- [x] Complete the CYSF portal

Review

Throughout the day, I made the finishing edits to all the sections of the CYSF portal. Most notably, I added missing images required as attachments, and I recorded my video in the evening. Lastly, I uploaded my logbook to the portal.

Additionally, I forwarded an email I received from the University of Calgary to Dr. Barber, Bhavana, and Britney, which mentioned that I would need to get my limited access associate account extended if I planned to continue working with them until the end of the year.



CL **Cole Lam** 12:16 PM

Fwd: General Associate & Associate - Limited Access - Expiring April/May/June 2025

To: Philip A. Barber, Britney Denroche, Bhavana Gill, Cc: Beatriz Garcia-Diaz Details

Hi all,

It looks like my Limited Access Associate is expiring on April 30th. In the case that I would continue working with you guys through to the end of the year, could you please extend my access?

Thanks!

Best regards,
Cole

Notes

None

Research Articles/Original Studies

Annotation Guide:

- Red: Key Effects/Outcomes
- Green: Key Vocabulary
- Blue: Statistics
- Brown: Other Key Information

Research Article:
A Classification and Outline of Cerebrovascular Diseases II[1] (Sept. 12-16, Incomplete)

- Introduction:
  - Purpose of the article is to classify known cerebrovascular diseases in a practical way that also includes diagnostic criteria
- Classification of Cerebrovascular Diseases:
  - Part 1: Clinical Stage:
    - Provides framework for describing the current status of a patient
    - Asymptomatic: classification for individuals with evidence of future cerebrovascular disease
    - Focal Cerebral Dysfunction: focal brain dysfunction regardless of nature
      - Transient (ischemic) attacks: see *White matter tract microstructure and cognitive performance after transient ischemic attack*
      - Actively changing neurological deficit: neurological deficit which is constantly changing or changed from its time of onset
      - Prolonged Neurological Deficit: generally stable neurological deficit
    - General Cerebral Dysfunction: general cerebral ischemia
      - Ischemia: inadequate blood supply to a vital organ
      - Transient: lasting for a short time
      - Prolonged: acute onset or progressive onset
  - Part 2: Pathophysiological Mechanisms:
    - Addresses the mechanisms by which diseases may change throughout their process
    - Primary abnormalities of cerebral circulation:
      - Thrombosis: coagulation/clotting of blood
        - Lysis: disintegration of a cell from the rupturing of the cell membrane
        - Recannulation: reinsertion of cannula (tubes) for administering medicine
      - Embolism: blocking of a vein or artery from a vessel too large to pass (fat, tissue, cancer cells, etc.)
        - Intraluminal source: from inside the esophagus
        - Cardiac source: from the heart
        - Other source: from somewhere else
      - Hemorrhage: bleeding from ruptured blood cells
      - Compression:
        - Change of position of head, neck or arm
          - Osteoarthritis: degenerative joint condition characterized by swelling and stiffness
          - Fibrous bands: elastic tissue in the lower legs and feet
          - Fracture: crack in a bone
        - Expanding mass
        - External forces (surgery)

        - Cerebral Edema: brain swelling
        - Acceleration
    - Vasospasm: narrowing of arteries
        - Post-traumatic
        - Migraine
        - Post-intracranial hemorrhage
        - Post-subarachnoid hemorrhage: bleeding in the protective layers of the brain
        - Hypertension: high blood pressure
            - Pheochromocytoma: tumor causing an excess of adrenaline
            - Acute Renal disease: cannot adequately filter blood in kidneys
            - Eclampsia: seizures during pregnancy from preeclampsia
                - Preeclampsia: high blood pressure and liver damage after pregnancy
        - Manipulation (surgery)
        - Embolism
        - Drugs
        - Other
    - Direction:
        - Reversal
        - Shunts
    - Alteration in rate or volume of circulation
        - Focal or general
    - Dissection of arterial wall
    - Associated with arteriography
        - Arteriography: visualization of an artery after injection or a radiopaque substances
- Primary abnormalities of general circulation
    - Hypotension: low blood pressure
        - Cardiac:
            - Rate, rhythm, conduction defects, myocardial impairment, valvular disease (prosthesis), pericardial disease (effusion)
                - Myocardial impairment: heart tissue impairment
                - Myocarditis: inflammation of the heart tissue
                - Valvular disease: heart valve failure
                - Prosthesis: artificial implant
                - Pericardial disease: disease of the pericardium (sac containing the heart)
        - Reflex:
            - Carotid sinus hypersensitivity: abnormal fall in heart rate in response to pressure applied on the carotid sinus
                - Carotid sinus: series of arteries in the neck
            - Vasovagal: fainting from overreacting to a stimulus
        - Shock
        - Blood loss:
            - Hemorrhage
            - Blood pooling
        - Orthostatic hypotension: loss of blood pressure from extended standing or sitting
        - Valsalva's Maneuver: forcefully exhaling with completely closed airways
        - Neurological diseases
        - Iatrogenic: illness related to drug intake/medical treatments

- Medication
- Post-sympathectomy: after the removal of the sympathetic nerve (causes sweating and blushing)
- Other vascular surgery

- Hypertension:
  - Medication
  - Emotional
  - Toxemia of pregnancy
  - Physical Exertion

- Alterations in blood:
  - Viscosity:
    - Dehydration
    - Overhydration
  - Cellular constituents:
    - Erythrocytes: red blood cells
      - Anemia: lack of sufficient red blood cells
      - Polycythemia: excess red blood cells
      - Hemoglobinopathy: disorders in the hemoglobin
        - Sicklemia: sickle cell disorder
        - Hemoglobin C
    - Leukocytes: white blood cells
    - Thrombocytes: platelets (that form plots)
  - Clotting defects:
    - Hypercoagulability: extremely quick clotting
    - Hypocoagulability: slow clotting
  - Proteins:
    - Macroglobulins: large proteins
    - Cryoglobulins: antibodies
    - Hyperfibrinogenemia: disorder with excess fibrinogens
      - Fibrinogens: blood clot protein
  - Lipids:
    - Cholesterol
    - Triglycerides
    - Lipoproteins
  - Glucose:
    - Hypoglycemia: not enough sugar
    - Hyperglycemia: too much sugar
  - Blood gases:
    - Oxygen
      - Hypoxia: not enough oxygen
        - Hypoventilation
      - Hyperoxia: too much oxygen
    - Carbon Dioxide
      - Hypocapnia: not enough carbon dioxide
      - Hypercapnia: too much carbon dioxide
    - Carbon Monoxide
    - Nitrogen
  - Metabolic demands:
    - Thermal changes:
      - Hypothermia: condition of being abnormally cold
      - Hyperthermia: condition of being abnormally hot
    - Convulsions
    - Medications
      - Barbiturates: hypnotic medicine for seizures
  - Predisposing factors:

        - Diabetes
        - Cardiac disease
        - Hyperlipidemia: abnormally high lipid disorder
        - Smoking
        - Hyperuricemia: excess uric acid
        - Obesity
        - Drugs
    - Part 3: Anatomy:
        - Two subdivisions: arteries (a, aa, v, vv) and central neural parenchyma
            - Central neural parenchyma: functional neural tissue
- Outline of Cerebrovascular Diseases:
    - Components:
        - Basic pathophysiological process causing a problem
        - Pathophysiological change in the brain parenchyma
        - Neurological abnormality impacting brain metabolism

Research Article: White matter tract microstructure and cognitive performance after transient ischemic attack (Sept. 10-12)[2]

- Vocab:
    - Transient ischemic attack (TIA): minor stroke
    - White Matter (WM): Network of nerve fibres (axons) which facilitates communication between the parts of the brain
        - Axons: Neuron extension that carries nerve impulses to other neurons
    - Diffusion Tensor Imaging (DTI): MRI technique that observes water diffusion in cells
    - Fractional Anisotropy (FA): Scalar value between 0-1, which measures the degree of anisotropy in diffusion processes
        - Anisotropy: Exhibiting properties where different values when measured are found in different directions
    - Mean Diffusivity (MD) Maps: visual representations of the mean diffusivity of data
        - Mean Diffusivity (MD): the mean diffusion, calculating using the three principal directions; calculated in tensor
            - Tensor: An algebraic object which shows the relationship between multiple vectors, scalars, or other tensors; frequently used for showing the relationship between x, y, and z axes
    - Adjusted Mixed Effects Regression: A regression representing binary data
    - Silent Brain Infarcts: Infarcts found through neuroimaging, without a previous history of stroke
        - Infarcts: Tissue death resulting from inadequate blood supply
    - Vascular Pathologies: where muscle cells stop working or die
    - Neurodegenerative Pathologies: where cells of the central nervous system (ie. neurons) stop working or die
    - Lesion: abnormal damage or change to a tissue
    - Heterogeneity: quality of being diverse
    - Mini-Mental State Examination (MMSE): 11 question test out of 30 points determining the subject's state of cognition
    - Framingham Risk Score (FRS): test used to predict cardiovascular disease (CVD)
    - Cardiovascular Disease (CVD): heart and blood vessel disease
    - Diffusion Weighted Imaging (DWI): MRI imaging where cellular rate of diffusion of water is used to create contrast in the imaging
    - Neuropsychological Battery: procedure assessing all major functional areas of the brain,

including those suffering from neurodegeneration
    - Montreal Cognitive Assessment (MoCA): test used to detect mild cognitive impairment; out of 30 points, where ≤25 indicates cognitive impairment
    - Addenbrooke's Cognitive Assessment-Revised (ACE-R): brief cognitive test out of 100, testing attention, orientation, memory, language, and verbal fluency
    - Brief Visuospatial Memory Test-Revised (BVMT-R): tests visuospatial memory
    - WHO/UCLA Auditory Verbal Learning Test (AVLT): an exam testing verbal recollection of words rapidly relayed to the subject
    - CLOX-1: a test used to identify executive impairment by asking subjects to draw clocks showing certain times
    - Trail Making Test A (TMT-A): a test of processing speed in which subjects are supposed to follow trails of numbers
    - Trail Making Test B (TMT-B): a test of executive function, using a similar tactic to TMT-A
    - National Adult Reading Test's (NART) Verbal IQ Score: a reading test which can also serve to show some level of IQ
    - Sagittal Plane: a vertical plane that passes through the body longitudinally (along the back and chest)
    - Transverse Plane: a horizontal plane that passes through the waist
    - Coronal Plane: a vertical plane that passes through the body (through the arms, parallel to the chest)
    - 3D Inversion Recovery Prepared Spoiled Gradient-Echo Sequence: ???
    - FreeSurfer: open source analysis and visualization tool for neuroimaging
    - Intracranial Volume (ICV): volume of the brain (inside the cranium)
    - MNI152 Template Space: ???
    - Cingulum Gyrus (CG): brain tract that processes emotion and behavior
    - Parahippocampal Cingulum (PHC): grey matter surrounding the hippocampus; plays a role in memory encoding and retrieval
    - Superior Longitudinal Fasciculus (SLF): largest associative fiber bundle of the brain
    - Uncinate Fasciculus (UF): white matter associative fibre
    - Fornix: white matter bundle, which plays an important role in the limbic system
        - Limbic System: interconnected brain structures regulating emotion and behavior
    - Corpus Callosum: white matter tracts that connect the left and right cerebral hemispheres
    - WM Hyperintensity: bright white spots within white matter
    - Skull Stripping: removing non-brain tissues from imaging
    - Cerebrospinal Fluid (CSF): tissue lining cavities in the brain
    - T-test: ratio comparing multiple means, considering variance and distribution
    - Wilcoxon rank-sum test: analysis of the ordering of data; useful when multiple outliers are present
    - Chi-Squared Test: test determining the probability that collected quantitative data and their corresponding trends were a result of chance
    - Fisher's exact test: test determining if the data proportions within categorical data were random
    - Linear mixed-effect (LME) models: regression analysis for dependent variables
    - Etiology: the cause(s) of a disease/condition
    - Partial Volume Effects (PVE): multiple tissues blur their tissue boundaries
- Introduction:
    - Current Understanding:
        - TIA has shown association with cognitive impairment, which in some cases cannot be explained through past stroke experiences (silent brain infarcts).
        - TIA has been known to increase the risk of dementia four times, but it is not well understood why (perhaps neurodegenerative pathologies and acute vascular lesions).
        - It is accepted that these diseases develop as early as decades prior to when symptoms are detectable.
    - Research Purpose:
        - To find an effective means of detecting neurodegeneration associated with TIA

before symptoms arise.
    - Expected Results:
        - Some relationship between WM microstructural variations and performance on neuropsychological tests.
        - DTIs yield results suggesting that they may serve as a biomarker of TIA
- Methods:
    - Sample:
        - TIA and non-TIA subjects aged 45-75
            - TIA subjects:
                - Underwent MRI scans and neuropsychological tests to confirm the presence of TIA.
            - Non-TIA subjects:
                - MMSE score between 24-30
                - No significant impairment in cognitive functions
                - No dementia
                - No depression
            - All subjects:
                - No other significant neurological diseases
                - No history of severe head trauma
                - No psychiatric disorders
                - No systematic illnesses
                - No substance abuse
                - No current use of sedating medications
    - Data collection:
        - Preliminary testing/requirements: clinical review, fasting cholesterol, glucose, renal function
            - Fasting cholesterol: fasting for 9-12 hours (no consumption of cholesterol
            - Clinical review:
                - Past medications
                - Sleep apnea (not enough oxygen)
                - Smoking, diabetes, cholesterol, blood pressure, etc used to compute the FRS
            - DWI intensity thresholds were calculated
    - Neuropsychological Battery:
        - Tested areas affected by stroke by assessing processing speed, verbal, and visual memory
        - Employed:
            - Cognitive tests: MoCA, ACE-R, MMSE
            - Memory tests: BVMT-R, WHO/UCLA AVLT
            - Executive Function tests: CLOX-1, TMT-B, DS Coding, TMT-A
            - Literacy: NART
    - Image Acquisition and Analysis:
        - Subjects underwent an MR scan , and had their anatomical images rendered along the sagittal plane.
        - Images were processed by FreeSurfer, looking at ICV among other factors.
        - Poor data was removed from the data set
    - DTI Tractography:
        - The CG, PHC, SLF, UF, fornix, and corpus callosum were observed (fibre density was considered)
        - DTI atlases were referenced to ensure anatomical accuracy for images.
            - Info like ICV were calculated
    - WM Hyperintensity Volume:
        - WM hyperintensities were measured.
        - Involved (to make the images easier to understand):
            - Skull Stripping

        - CSF removal
        - WM segmentation
    - Statistical tests:
        - Analyzed mean, SD, median, frequency distributions
        - Tests included:
            - T-tests
            - Wilcoxon rank-sum test
            - Chi-Squared tests
            - Fisher's exact tests
- Results:
    - Demographics:
        - 95 TIA patients (all TIA) had small lesions
        - TIA patients scored lower on ACE-R (lower attention, memory,
    - Association of TIA with FA (fractional anisotropy) and MD (mean diffusivity):
        - Related to WM traits
        - TIA subjects had lower FA and higher MD
    - DTI FA and MD with neuropsychological test scores:
        - Lower FA and higher MD generally led to poorer performance on tests, with the exception of the TMT-B time component of the test
- Discussion:
    - TIA subjects exhibited differences in DTI measures (damaged microstructure)
    - Higher MD values in the fornix, lower FA values
    - No relationship between DWI lesions and DTI measurements
    - TIA subjects showed generally lower cognitive outcomes, especially in memory, executive function, processing speed
    - Cognitive changes may indicate vascular and Alzheimer's Disease (AD) pathology
    - All of the tracts that impacted by TIA seem to have impacted memory
    - Changes in FA and MD in the SLF suggested changes in cognitive function (and was supported in the experiment)
        - Relates to the deterioration of the brain resulting from normal aging
    - Limitations:
        - PVE could also have caused lower FA and higher MD values
    - Conclusion: analyzing WM deterioration using DTI could help predict neurodegenerative and cerebrovascular diseases prior to cognitive impairment
- Summary:
    - The purpose of the tests were to determine alternate ways of predicting neurodegenerative before cognitive decline is observable.
    - Done by observing white matter tract microstructures for patients with transient ischemic stroke
    - Included 95 TIA patients and 51 non-TIA patients, who underwent cognitive tests (neuropsychological battery), and were also assessed using diffusion tensor imaging.
        - Specifically, mean diffusivity and fractional anisotropy data were collected.
    - Using FreeSurfer, DTI images were analyzed and processed to observe changes to the brain, including lesions, and other values such as FA and MD.
    - Data showed that TIA patients exhibited higher MD values and lower FA values, which was associated with lower memory and executive function.
    - The conclusion was that analyzing WM deterioration could be a means of detecting neuro degenerative diseases, and using DTI specifically could do this effectively. However, further investigation would be necessary to draw a conclusion.

Research Article:
A longitudinal magnetic resonance imaging study of neurodegenerative and small vessel disease, and clinical cognitive trajectories in non demented patients with transient ischemic attack: the PREVENT study (Sept. 16-18)[3]

- Vocab:
  - Small vessel disease (SVD): where the walls of arteries do not function properly, inhibiting blood flow to the heart
  - Alzheimer's Disease (AD): most common form of dementia
  - Vascular Dementia (VaD): cerebrovascular dementia; also known as small vessel cerebrovascular disease
  - Effect size: the magnitude of the difference between groups
  - Ataxia: loss of muscle control
  - Diplopia: double vision
  - Hemianopia: loss of half of the vision field
  - Apolipoprotein E (APOE) genotyping: evaluating DNA for APOE alleles (a risk factor for AD and VaD)
  - Cerebrospinal Fluid (CSF): biomarker for AD, cushions brain in skull
  - Tau: protein stabilizing neuron skeletons
  - Amyloid $ß_{1\text{-}42s}$: implicates AD
  - Quantitative Susceptibility Mapping (QSM): MRI technique for analyzing spatial distributions of magnetic sensitive cells
  - Random Forest Model: using decision trees to make predictions by determining the most common output
  - Support Vector Machines: used for performing linear classification
  - Deep Neural Networks: artificial neural networks with many layers, often hidden
  - Quadratic Inference Function Classifiers: ???
- Introduction:
  - Current Understanding:
    - Late-life cognitive decline (neuronal loss leading to brain atrophy) is expected to increase vastly between 2018-2038.
      - Associated with AD and VaD
    - Patients with TIA often display signs of neurodegeneration, and are four times more likely to develop dementia.
    - However, if neuronal loss can be detected earlier on before symptoms are detected, effective prevention is possible.
    - Covers what disease processes lead to neurodegeneration, cognitive decline, and brain atrophy.
  - Research Purpose:
    - To determine if measurements of brain iron accumulation can predict brain atrophy and cognitive decline.
- Methods:
  - Aims to achieve a 30% group effect size between TIA and non-TIA patients regarding cerebral atrophy
  - 220 TIA patients and 220 non-TIA patients
    - TIA patients' criteria:
      - Documented TIA with symptoms
      - No dementia
      - MR for determining DWI lesion
      - $45 \leq \text{age} \leq 75$
      - English fluency
      - No substance abuse/alcoholism
      - No other preexisting diseases

        - Non-TIA patients' criteria:
            - No prior stroke experiences
            - No dementia
            - No other preexisting diseases
    - Data collection:
        - Includes clinical review, fasting cholesterol and glucose tests
        - Treatments for hypertension, hyperlipidemia, etc. will be determined
        - APOE genotyping will be performed to predict potential AD and VaD
        - Constant BP measurements, including at home
        - CSF, tau, and amyloid $ß_{1-42}$ are collected
    - Image Acquisition:
        - MR scans are taken at the Y0, Y1, and Y3 marks
        - DWI is performed (observing for abnormal cells)
        - Brain and hippocampal volume change is calculated using T1-weighted images (short MRIs)
        - QSM measurements were acquired
    - Neuropsychological Assessments:
        - Cognitive tests were assessed at baseline and then annually, looking for change over time.
    - Statistical Analyses:
        - Compares mean, median, S_x, frequency
        - Mixed repeated measure regression model used for comparing z-score measures at Y0, Y1, and Y3.
        - 95% confidence interval
        - Prediction models are based on machine learning
            - Utilized random forest models, support vector machines, deep neural networks, and quadratic inference function classifiers
- Discussion:
    - Points out the importance of focusing on high-risk populations and standardized biomarkers for the prevention of dementia
    - The PREVENT study hopes to support the idea that rate of cerebral atrophy is a meaningful measure of disease progression
        - The study is (was) still in progress, performing clinical evaluations, cognitive tests, and MRs yearly
        - Continuing with the study, the priority will be on individuals who have the highest risk of developing dementia.
- Summary:
    - Late-life cognitive decline is becoming increasingly common, which is associated with a four time higher risk of developing dementia
    - The PREVENT study aims to find ways to detect cerebral atrophy before symptoms arise in order to prevent dementia
    - The study is conducted with 220 TIA and non-TIA patients each, and testing includes clinical testing, as well as MR assessments, neuropsychological, and fluid biomarker testing on a yearly basis.
    - By the time this article was published, the PREVENT study had not been finished, but continued to aim to find ways to prevent dementia in individuals aged 45-75, prioritizing those with a higher risk.

Research Article:
Population-based blood screening for preclinical Alzheimer's disease in a British birth cohort at age 70[4] (Sept. 24, Incomplete)

- Vocab:
  - Cerebral Amyloid-β Deposition: accumulation of amyloid beta-peptides in cerebral blood vessels
    - Amyloid-β Peptide: an amino acid-peptide that is an initiator of AD
  - Liquid Chromatography-Mass Spectrometry: technique for determining the quantities of different substances in a liquid sample (in this case, blood sample)
  - Single Molecule Array (SIMOA): technique for quantifying protein biomarkers in serum, plasma, or CSF
  - ^{18}F-florbetapir Amyloid PET Positivity:
    - Amyloid PET Positivity: the taking of a PET in order to distinguish diseased tissues from healthy ones
      - Positron Emission Tomography (PET): scan for analyzing the metabolic functions of tissues
    - ^{18}F-florbetapir: a compound associated with AD pathogenesis
  - Apolipoprotein E (APOE): a protein that combines lipids to create lipoproteins
    - APOE gene: the gene associated with providing instructions for creating APOE proteins, with ε2, ε3, and ε4 being the three potential alleles
      - ε3 is the most common with over 50% of the population having it
      - APOE ε4: APOE gene associated with higher risk of AD
  - Covariate: an independent variable that is observed, but is not the focus of the study
  - Coagulopathies: condition where the body's ability to clot blood is impaired
- Introduction:
  - Current Understanding:
    - AD has a preclinical stage of cerebral amyloid-β peptide, in which targeted therapies have the maximum impact. However, current measurement techniques of amyloid-β are difficult to deploy at scale, so the alternative is blood screening.
    - Amyloid PET is effective, but expensive, and CSF sampling poses the risk of coagulopathies.
  - Research Purpose:
    - This study aims to use liquid chromatography-mass spectrometry, SIMOA, and phospho-tau181 techniques to detect ^{18}F-florbetapir amyloid PET positivity.
    - Age, sex, and APOE ε4 as covariates
- Methods:
- Discussion:
- Summary:
  -

Research Article:
Mixed brain pathologies account for most dementia cases in community-dwelling older persons[5] (Sept. 18, Incomplete)

- Vocab:
  - Lewy Body Disease (LWD): progressive dementia impacting the ability to think, reason, and process information
  - Pathogenesis: development of a disease
- Introduction:
  - Current Understanding:
    - Previous studies of neuropathology in community/population based cohorts have previously shown AD as the most common cause of dementia, leading to LWD, and, less commonly, frontotemporal dementia.
    - However, past studies often cannot be generalized to the community or general population of the elderly.
  - Research Purpose:
    - To examine the spectrum of neuropathology within a certain cohort

NIH Summary:
APOE gene: MedlinePlus Genetics (Sept. 30)[6]

- What is the role of the APOE (Apo-E) gene:
  - The APOE gene provides instructions for producing apolipoprotein E (APOE).
    - Apolipoproteins are fat-binding proteins
  - APOE combines lipids to create lipoproteins, which packages fats for transport through the bloodstream.
  - APOE plays a significant role in maintaining cholesterol levels, in order to prevent cardiovascular diseases and neurological disorders
    - In the brain, APOE is the lead carrier of cholesterol
  - The APOE gene has three alleles: ε2, ε3, and ε4
    - ε2 is a protective factor against AD
    - ε3 is most common in people (>70%)
    - ε4 is a risk factor for late-onset sporadic AD (those with a copy of the ε4 allele are more likely to be at risk of developing AD)
      - Those with two copies of the ε4 allele are even more likely to develop late-onset AD than those with one copy.
      - Those with the ε4 allele may also experience earlier onset of memory loss and other AD symptoms
  - Currently, it is unknown why APOE is associated with sporadic AD
    - The only current correlation between APOE and brain structure is the presence of amyloid plaques, where amyloid-β peptides are accumulating in brain tissue
  - The APOE gene has also been discovered to be associated with the development of Lewy Body dementia.
    - Lewy Body dementia is associated with intellectual decline, hallucinations, tremors and limb rigidity, and other symptoms of Parkinson's disease
    - Current theory suggests that APOE may disrupt the transport of α-synuclein proteins, accumulating lewy bodies in cells
    - The accumulation of lewy body proteins causes neuron function to become impaired

Research Article:
APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches.[7] (Sept. 26-30, Incomplete)

- Vocab:
  - Sporadic AD: most common form of AD
  - Amyloid-β (Aβ) Peptide Aggregation: increased concentration of amyloid-β peptides
    - Amyloid-β Protein: glycoprotein that produces peptides (specifically, Aβ40 and Aβ42)
    - Peptide: a compound of amino acids
  - Tau Neurofibrillary Degeneration: degeneration resulting in neurofibrillary tangles
    - Neurofibrillary Tangle: abnormal accumulations of tau in neurons
      - Tau: protein that stabilizes the internal skeleton of neurons
  - Microglia: brain immune cells that are in constant motion
  - Astrocyte: brain immune cells that are planted in tissues
  - Blood-brain Barrier Disruption: use of drugs to create openings between cells in the blood-brain barrier
    - Blood-brain Barrier: network of blood cells to prevent harmful substances from reaching the brain
- Introduction:
  - Current Understanding:
    - APOE ε4 is one of the strongest genetic risk factors for sporadic AD
      - Linked to amyloid-β peptide aggregation, tau neurofibrillary degeneration, microglia and astrocyte responses, and blood-brain barrier disruption
    - APOE ε3 is the most common allele for APOE
    - APOE ε2, the rarest allele, is also a strong genetic protective factor for sporadic AD, emphasizing the significance of the APOE gene and APOE proteins on the pathogenesis of sporadic AD.
    - However, there are currently no targeted treatments to address APOE disorders
- Methods:
- Discussion:
- Summary:
  -

Research Article:
Vascular Risk Factors: Imaging and Neuropathologic Correlates (Oct. 3)[8]

- Vocab:
  - Vascular Risk Factor (VRF): a factor that increases the chance of developing vascular dementia (VaD)
  - Diabetes Mellitus (DM): diabetes associated with abnormally high glucose levels
  - Hypertension (HTN): abnormally high blood pressure
  - Hypotension: abnormally low blood pressure
  - Hyperlipidemia (HLD): abnormally high cholesterol
- Content:
  - Cerebrovascular dementia (CVD) and AD both impact elderly populations, and make up mixed vascular-Alzheimer dementia (MVAD)
    - Within this, they have overlapping risk factors
  - Stroke is often associated with CVD and has had impacts relating to AD within MVAD
    - Especially through strokes, cognitive impairment has had impacts on AD
  - VRFs:

        - DM:
            - DM has had a stronger association with CVD, because cognitive decline has become associated with DM
            - DM can cause structural changes to the brain, particularly brain atrophy
        - HTN:
            - HTN is a risk factor for ischemic heart disease, peripheral vascular disease, etc.
            - Hypotension in late life has similar deleterious effects on brain structure as HTN
            - HTN (and hypotension) can cause brain atrophy, hemorrhage, and strokes
        - Obesity:
            - Has been found to be a VRF, but its association with dementia is currently unknown
            - Persists alongside other VRFs, such as DM, HTN, and hyperlipidemia
        - HLD:
            - Elevated cholesterol levels has found to be associated with VaD
            - Hypercholesterolemia has been a proven risk factor for cardiac disease, although has been inconsistent with regards to CVD
            - My comment: HLD may be associated with AD with regards to APOE and its impact on AD
- Summary:
    - My previous knowledge: Within MVAD, VRFs overlap between the different types of dementia (AD, CVD)
    - VRFs include DM, HTN and hypotension, obesity, and HLD, which typically result in brain atrophy associated with VaD, and by extension AD
        - VRFs like DM, obesity have associations with CVD and AD that are not fully understood
    - Treatment of VRFs can be successful in mid-life but are practically incurable in late life

Research Article: What are White Matter Hyperintensities Made of? [9] (Oct. 8-10, Incomplete)

- Vocab:
    - White Matter Hyperintensities (WMH): hyperintense (bright white) spots visible on brain MRIs
    - Magnetization Transfer Ratio (MTR): observes the function for cells to exchange magnetizations with macromolecules
    - Content:
        - WMHs, although initially regarded as an inevitable consequence of aging, has been associated with a triple risk of stroke and double risk of developing dementia
        - Very commonly found in MRI and CT scans
        - Most knowledge right now about WMHs is from post-mortem autopsies, leading scientists to believe that WMHs are generally associated with late-onset neuropathologies
    - Historical Perspective:
        - About 15 million people have stroke every year
        - WMHs were first observed in CT scans with hyperintense spots on brain scans
        - Before this, WHMs were generally ignored (thought to bear no significance)
    - Current clinical significance:
        - WMHs increase in prevalence with increasing age, although its presence generally indicates progressive cognitive impairment
            - Impacts physical function and cognition
            - Associated with a higher risk of developing depression
        - **WMHs are heritable**

- VRFs increase the prevalence of WMHs (smoking, diabetes, obesity, etc.)
- **Some studies have revealed that high cholesterol levels were the most significant risk factor for WMHs in elderly**
- DM has been found to be the most common risk factor for WMHs in younger populations
- Physical activity (exercise) has shown to protect (to some extent) against WMHs

- What is it:
  - WMHs are part of the SVD spectrum, which includes lacuna strobes, ischemic or hemorrhagic stroke, and brain atrophy.
  - WMHs are associated with cortical thinning and cerebral atrophy → progressive brain damage
    - All effects of WMHs are cumulative
  - Associated with demyelination and axonal loss (permanent brain damage)
  - WMHs have shown to exacerbate the severity of other neuropathologies
- How are they observed:
  - Typically observed in MRIs and DTIs
    - Parameters include FA and MD
  - MTR is an MRI biomarker for white matter damage which can be associated with WMH

- Summary:

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Background Research

(Jan. 21 - Feb. 13)

1. Neurological Disorder Prevalence

As societies have developed throughout the epidemiological transition model, the onset of neurological disorders has increased. Specifically, these disorders were responsible for approximately 10 million deaths worldwide in 2019.[1] Notably, stroke is a leading cause in a decrease in disability-adjusted life years (DALYs), with other causes including Alzheimer's Disease (AD), Parkinson's Disease, dementia, and meningitis.[1] Focusing in on Canada, where technological advancements have made neurological disorders more common than infections and other chronic disorders, nearly 600,000 individuals were estimated to be living with a form of dementia.[2] This value is also estimated to increase to over 1.7 million by 2050, illustrating the developing prevalence of these disorders.[2]

At a regional level, North America, and Western and Eastern Europe were found to have the highest incidence rates of neurological disorders in 2019.[1] This is consistent with levels of technological developments within the health industry, as higher life expectancies generally coincide with the manifestation of such disorders. Despite this, East Asia and Central America have experienced the greatest rates of increase, particularly with regard to Alzheimer's disease and similar dementias.[1]

With regard to differences between age, race, and sex cohorts, studies have revealed trends that suggest an uneven proportion of dementia patients across different cohorts. In a published manuscript summarizing demographic trends presented at the *2020 National Research Summit on Care, Services, and Supports for Persons with Dementia and Their Caregivers*, *Theme 1: Impact of Dementia*, findings included that a larger absolute value of white Americans presented with Alzheimer's disease and related dementias (ADRD), although Latinos and African Americans are disproportionately more likely to develop ADRD compared to white Americans.[3] The potential explanations for these trends are complex; stress resulting from low socioeconomic statuses coupled with discrimination are suspected to be one of the causes.[3] Irrespective of the subgroups, statistics have also suggested a higher prevalence of ADRD cases in women than in men with a 0.9 male-to-female ratio worldwide, and that ADRD proportions increase with advancing age.[1,3] In fact, all ethnic subgroups experienced over a 30% increase in proportion of ADRD individuals between age groups 65-74 and 85 and older.[3]

However, regardless of variability of risk between the age, sex, and ethnic cohorts, the rising prevalence of these disorders worldwide emphasizes the importance of scientific research that can improve diagnostic processes and patient prognosis. Overall, recent rapid development in

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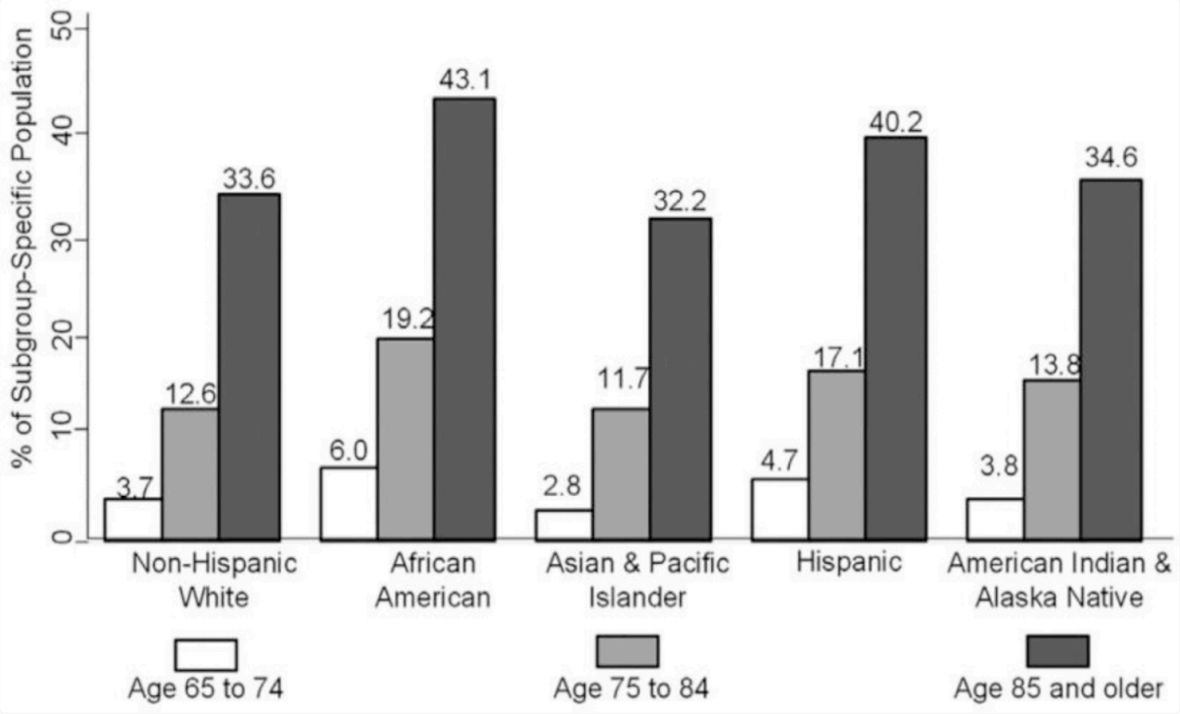

Estimated prevalence of Alzheimer's disease and related dementias in the US Population aged ≥65 years, by sex and race and ethnicity; United States, 2014.

treatments for neurological disorders have increased in quality with regard to surgical, pharmacological, and interventional treatments, but the early onset of neurological disorders that cause nerve damage early in life means that patient prognosis is overall quite poor.[1,4] This ultimately emphasizes the importance of preventative treatments, which requires advancements in accurate early diagnosis of cognitive decline.

2. Common Manifestations of Cognitive Decline

2.1. Alzheimer's Disease (AD) and Related Dementias

Alzheimer's Disease (AD) is the most common form of dementia, comprising 60-70% of diagnosed dementia cases.[2] The development of AD is suspected to be 60-80% contingent on nonmodifiable genetic factors, in which more than 40 loci have been identified to be potentially significant; among those, the APOE alleles have shown to present the greatest risk in patients.[5] Regardless, onset of AD physiologically is most prominently characterized by changes in amyloid-β (Aβ) and tau concentrations (See: 3.2. Cerebrospinal Fluid (CSF)) which often begin decades before observable cognitive symptoms are noticeable.[4,5]

The clinical spectrum of AD manifestations is quite broad, in which the process of diagnosis varies from patient to patient. More commonly, AD can be determined through the analysis

of cognitive function, and is often corroborated by genetic analysis, such as analyzing cerebrospinal fluid (CSF) protein concentrations, assessing genes such as APOE, and evaluating for mutations such as PSEN1 which influence the production of Aβ proteins.[5] Brain MRI or CT scans are also commonly taken, which can reveal abnormalities in brain tissues, such as white matter hyperintensities, perivascular spaces, cerebral microbleeds, and small subcortical strokes.[6] Symptoms of AD include short, long, and self-perceived memory loss, loss of multitasking ability, and progressive difficulty of understanding words and forming coherent sentences among others, but because symptoms often do not present under early stages of brain atrophy, early diagnosis is more complicated.[5]

Another specific branch of dementia, vascular dementia refers to a decline in cognitive function resulting from vascular brain injury, resulting in impairment.[7] Although symptoms are consistent with other forms of dementia such as AD, its development is primarily identifiable through brain scans that observe abnormalities in brain structure.[8] The most common vascular risk factors are cardiovascular, including diabetes mellitus, hypertension, hyperlipidemia, and smoking.[7] In the amplification of these vascular risk factors, outcomes include ischemic strokes, haemorrhagic strokes, and cerebral small vessel disease (CSVD), among others. Ischemic strokes are characterized by artery blockages within the brain, whereas haemorrhagic strokes involve strokes from excessive bleeding in the brain.[7] CSVD is a common manifestation of vascular dementia, which is identifiable by abnormal structures in MRI and CT scans.[4] Specifically, the presence of white matter hyperintensities, perivascular spaces, microinfarcts, and cerebral microbleeds indicate the onset of CSVD and contribute to cognitive decline, alongside other harms.[9]

It is important to note that the majority of dementia cases worldwide are not strictly AD or vascular dementia or any single form of dementia; rather, cases are mixed, where a variety of risk factors contribute to a mixed dementia where patients experience cognitive decline from many areas, not limited to genetics, vascular factors, or protein concentrations.[10] The most common forms of mixed dementia are characterized by the coexistence of AD and vascular dementia, which makes treatment difficult.[11] Addressing the number of different factors that contribute to cognitive impairment requires a focus on many separate systems, which ultimately explains why treatment is often circuitous for patients with fully-developed dementia.[2]

2.2. Transient Ischemic Attacks (TIAs)

Transient ischemic attacks (TIAs) are characterized by minor disruptions to the blood flow in the brain.[12] Compared to ischemic strokes, blood flow does not experience a complete blockage, but rather, a reduction, which most commonly results in sporadic symptoms that do not exceed 24 hours in length.[4] These symptoms include partial weakness and paralysis of the face, slurred speech, and dizziness, but because of the short duration of these

symptoms, their occurrence was often not considered to be significant.[13] However, studies have shown that TIAs are incontrovertibly correlated with mid to late-life cognitive impairment, and can predict future cognitive decline.[4,12,14] In fact, approximately 11% of individuals who experience a TIA and are untreated within 7 days develop acute ischemic stroke, and this number increases to 18% after 90 days.[15] On the whole, TIAs are predicted to precede significant changes to brain structure and function that result in AD and related dementias, so on that basis, TIAs can serve as a predictive marker for the onset of cognitive decline. Especially considering the difficulty of treating AD and related dementias once fully developed, the use of TIAs to predict early brain changes is incredibly useful in identifying cognitive decline and implementing preventative practices as early as possible.

Much of current focus on TIAs has been into practical means of diagnosis, which tend to be more difficult than more developed brain changes, notably because the magnitude of any changes are much less.[12] Because symptoms are short-lived, it is a less reliable means of diagnosis, so other methods such as MRI/CT brain scans tend to be more commonly used.[12] For individuals who are presented with a TIA, small lesions or hyperintense spots often appear in scans, which helps support evidence of TIA occurrences. Overall, treatment for TIAs is similar to that of ischemic strokes. Considering that TIAs represent a less severe manifestation of ischemia, the application of existing knowledge in ischemic strokes is useful when addressing TIAs, including the prescription of antiplatelet agents.[12]

Other research has suggested that TIAs can be used to predict dementia and overall cognitive decline. Much of this evidence is suggested in analyzing trends, in which individuals who experienced minor strokes such as TIAs later gradually experienced cognitive decline leading to dementia.[16] Additionally, analysis of brain scans of TIA patients shows similarities in the manifestation of AD and related dementias, as hyperintense spots identified on brain scans are similar to those that present in dementia patients.[16] However, any analysis into the role of other cognitive risk factors, such as genetics and cerebrospinal fluid (CSF) has been limited. Most analysis has focused on the role of vascular risk factors and physiological brain changes, which provides an opportunity to further explore the associations between TIA and AD and related dementias.

3. Current Advancements in Diagnosis

3.1. Brain Imaging Techniques

Because the development of neuropathologies begins long before symptoms are identifiable, the use of brain scans, including computer tomography (CT) and magnetic resonance imaging (MRI) scans, are incredibly useful to detect early brain changes. CT scans are characterized by the use of X-rays, which allow for a high resolution of brain scans.[17] However, MRI scans, which use radio waves, better visualize contrast, which tends to be

more useful in identifying hyperintense abnormalities on the brain.[18] Another brain scan that is commonly coupled with either MRI or CT scans are positron emission tomography (PET) scans, which use an injected radioactive tracer to track bodily and metabolic functions. With regard to cerebrovascular diseases, PET scans are useful in identifying tumours, senile plaques (amyloid-β plaques), and other brain function abnormalities.[19]

In analyzing brain scans, one of the major focuses are areas that appear abnormal or hyperintense, making MRIs a top choice for analyzing demented patients. Indications of white matter hyperintensities, cerebral microbleeds, perivascular spaces, and microinfarcts, for instance, are valuable in diagnosing CSVD in predicting cognitive decline.[9] The presence of senile plaques (ie. amyloid-β plaques) can also be identified on brain imaging scans, which explains their popularity in usage to diagnose and analyze cognitive impairment in patients.[20]

3.2. Cerebrospinal Fluid (CSF)

Cerebrospinal fluid (CSF) is a valuable cognitive biomarker that has become increasingly common in diagnosing AD and related dementias. CSF is produced by the choroid plexus, a ventricle of the brain, and is present in intracranial and spinal compartments, largely responsible for cushioning the brain and nerves, meaning it directly interacts with the extracellular surfaces of the brain.[21] Additionally, CSF plays a role in the transfer of nutrients and proteins throughout the nervous system, making it a valuable area to study with regard to cognitive impairment.[21] CSF is collected most commonly via a lumbar puncture, a procedure where a needle is inserted into the subarachnoid space within the spinal canal to collect a fluid sample.[22] After collection, cerebrospinal fluid is a generally reliable biomarker in diagnosing acute brain conditions, including subarachnoid haemorrhage, meningitis, amyotrophic lateral sclerosis, and dementia.[21] The detection of these conditions is identified largely through a composition analysis, which looks at microRNA, neurofilament light chains (NFL), and proteins, including amyloid-β peptides and tau proteins.[21] However, in detecting AD and related dementias, the analysis of amyloid-β (Aβ) peptides and tau proteins is most relevant.[21]

Aβ peptides are cleaved from amyloid precursor proteins (APP), which are notably prevalent in the synapses of neuron cells.[23] APP is largely responsible for neuronal development and signalling, but when they misfold or produce abnormal Aβ peptides, they produce Aβ senile plaques that inhibit neuronal function.[23] Over the long term, Aβ peptide production increases with age, resulting in greater aggregates of senile plaques as the brain ages.[24] Although the direct impact of Aβ peptides on cognitive decline is currently unknown, Aβ has been determined to be a valuable biomarker that can be used to aid the diagnosis of neurodegenerative disorders, so much so that its presence in senile plaques has become a hallmark characteristic of AD and some related dementias.[20,23] The two most prevalent

forms of Aβ are the 40 (Aβ 1-40/Aβ40) and 42 (Aβ 1-42/Aβ42) amino acid chains.[20] The difference between Aβ40 and Aβ42 peptides is the presence of two additional C-terminal residues on the Aβ42 peptide, and this difference causes Aβ40 and Aβ42 to have very different implications on cognitive impairment.[25] Specifically, while Aβ40 is much more abundant in the brain, it tends to be less common in senile plaques.[25] This is largely suspected to be due to the greater tendency for Aβ42 to aggregate from having a larger molecule size, and it is for this reason that Aβ42 is generally a more valuable biomarker of cognitive impairment.[25] However, Aβ40 serves as a relevant comparison to Aβ42, as lower Aβ42/Aβ40 values have been associated with steeper senile plaque accumulation and greater cognitive decline.[26] Aβ42 is also a valuable biomarker irrespective of Aβ40 concentrations.[20] On the whole, Aβ42 concentrations in CSF are strongly negatively correlated with the density of senile plaques in brain tissue; in other words, lower concentrations of Aβ42 in CSF samples are generally associated with higher Aβ senile plaques. This correlation has proven useful in predicting levels of cognitive impairment, given that high densities of Aβ senile plaques is an accepted characteristic of AD and related dementias. However, further research has revealed that even after accounting for this correlation, Aβ42 concentrations in CSF samples still tend to be lower in cognitively impaired individuals than normal controls, which ultimately strengthens the associations between low Aβ42 concentrations and levels of cognitive impairment. Overall, the use of Aβ as a biomarker for neurodegenerative diseases has proven useful, although studies have suggested that Aβ in isolation does not drive cognitive decline, and thus may not be sufficient in predicting the implications of cognitive impairment.[24]

Tau proteins are responsible for the stabilization of the cytoskeleton of neurons under standard physiological conditions.[27] Specifically, tau is known to maintain the integrity of the microtubules of the neuron cytoskeleton, but mutations and structural modifications that occur with advancing age often result in neuronal dysfunction and neurodegenerative disorders, known as tauopathies.[27] Unlike Aβ, the manifestations of disorders (tauopathies) caused by modified tau are known to directly influence and accelerate cognitive impairment, especially as hyperphosphorylation occurs.[24] Compared to healthy controls, studies have revealed that tau is three to four more times phosphorylated in demented patients, which ultimately depresses the level of tau activity and results in greater production.[28] Because of this, total tau (t-tau) and phosphorylated tau (p-tau) are valuable CSF protein biomarkers that clinicians often analyze when a patient presents with symptoms of cognitive impairment. Patients with developed cognitive impairment in the form of AD and other forms of dementia most commonly present with elevated levels of both p-tau and t-tau.[29] Although the reasons for elevated p-tau levels are not fully understood, studies have revealed that a higher concentration of p-tau results in a decrease in functionality, causing a greater production of tau (t-tau) in the brain.[29] This trend is identifiable in CSF samples, although in very small amounts, but nonetheless, is valuable in the diagnosis of neurodegenerative disorders.[28,29]

Analysis of the ratios between Aβ and tau concentrations also provides another layer of analysis in establishing cognitive impairment. For instance, the analysis of t-tau/Aβ42 can help further establish the severity of neurofibrillary tangles and Aβ senile plaques in the brain, as higher values of this ratio generally correspond with more severe cognitive decline.[30] Although t-tau is individually suspected to rise with cognitive impairment alongside decreasing Aβ42 concentrations, this ratio is particularly valuable because it illustrates the interaction between the varying concentrations, which can provide clinicians with a better idea of what specific brain changes are occurring.[30] Similar to the t-tau/Aβ42 ratio, p-tau/Aβ42 provides similar information about the extent of cognitive impairment based on the two CSF protein biomarkers. Although measuring similar values to the t-tau/Aβ42 ratio, the analysis of p-tau/Aβ42 is particularly useful for analyzing the severity of tau phosphorylation which is more notably associated with AD.[30]

When used in conjunction with each other, the analysis of tau and Aβ concentrations is powerful in predicting the extent of cognitive decline in an individual, and the expected implications of the disorder; longitudinal memory decline has been noted to decline most severely with elevated tau and Aβ concentrations, for instance.[24] However, most of the analysis regarding the role of CSF biomarkers in influencing cognitive impairment has been focused on AD and related dementias, as which point cognitive impairment has already significantly developed. Research into earlier indications of cognitive decline, such as TIAs, comparatively, has not been thoroughly explored, and potentially provides the opportunity to better understand the significance of CSF protein biomarkers.[4]

3.3. Blood Tests

In assessing the genetic biomarkers that can contribute to cognitive impairment, blood tests are valuable for establishing nonmodifiable risk factors in understanding the manifestation of cognitive decline in individuals. Although blood tests can isolate plasma to assess Aβ, tau, and NFL, assessing genes through blood tests tend to be more popular, as the analysis of CSF samples tend to provide more valuable results.[31]

Among the known genetic risk factors that contribute to AD and related dementias, the apolipoprotein E (APOE) genotype is one of the most popular factors to assess. Independent of its impact on cognitive decline, the APOE genotype is responsible for producing apolipoproteins which combine lipids to regulate cholesterol levels.[32] This is generally important for preventing cardiovascular diseases and vascular dementia, given APOE is the primary carrier of cholesterol in the brain. Despite this, research has revealed that the different polymorphisms of the APOE genotype tend to protect individuals from AD and related dementias, or increase their risk of cognitive decline.[33] Although the reasons for the correlation are not well understood, Aβ senile plaque concentration has been observed to

vary within demented individuals with different APOE polymorphisms.[34] The APOE genotype presents with three different alleles: ε2 (APOE2), ε3 (APOE3), and ε4 (APOE4).[34] The APOE3 allele is the most common in individuals, with a 0.779 allele frequency, while the APOE2 allele is the most rare, with a 0.084 frequency.[35] Between the three alleles, the ε3 allele is known to not present with any risk or provide any protection against cognitive decline, but the ε4 allele has shown to be associated with greater densities of Aβ plaques and cognitive impairment. Specifically, research has revealed that APOE4 homozygosity is associated with the highest risk of cognitive impairment of all APOE polymorphisms, but individuals with at least one ε4 allele still present a higher risk of dementia than other individuals.[4] Comparatively, the rarer ε2 allele is suspected to protect against cognitive decline.[34] In clinical practice, the APOE4 alleles are of greatest focus and are most valuable in assessing cognitive impairment risk. Although APOE cannot be used to independently diagnose dementia, it is a valuable predictor that can corroborate other evidence relating to cognitive impairment onset.

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Ethics Courses

Ethics Course:
TCPS 2: CORE-2022 (Oct. 13-17) TCPS 2: CORE-2022)

- Summary:
    - TCPS Fundamental Value: **Respect for Human Dignity**
    - TCPS Core Principles:
        - Respect for persons
            - Each person has an intrinsic value
            - When conducting research, subjecting a patient to the risks of participation must be fully voluntary
        - Concern for welfare
            - It is important to avoid exposing patients to unnecessary risk
        - Justice
            - Dual obligation for all parties to treat others equitably and fairly
            - Burdens for participants must be equally distributed in determining any intervention
            - Important questions:
                - Why this specific group of prospects, and not narrower or broader?
                - Is there a sound and logical reason to conduct this research?
                - What are the risks and who will they impact?
    - Ethics and law must be balanced, without compromise to law
        - If there are conflicts (but are rare), you need to anticipate the problems and try to design the research so that it maintains consistency between ethics and law.
        - Consulting colleagues can be helpful
    - Who is responsible for the TCPS:
        - Created in 1988
        - The Secretariat on Responsible Conduct of Research (SRCR): drafts, revises, interprets and helps implement the TCPS
        - The Panel on Research Ethics (PRE): provides expert, independent advice on the content of the TCPS
        - **Anyone conducting research under the auspices of eligible institutions are obligated to follow the TPCS who are working with human subjects**
            - Generally, all universities, colleges and hospitals sign the agreement
        - Tri-Agency Framework: Responsible Conduct of Research (RCR Framework) describes the responsibilities of all parties with regard to the TCPS
        - Violations of the TPCS can result in letters of awareness to an inability to gain funding from agencies
    - Conducting Research:
        - All research involving human subjects must be ethically reviewed and approved by the research ethics board (REB)
            - Research: an undertaking intended to extend knowledge through a disciplined inquiry and/or systematic investigation
            - Disciplined Inquiry: inquiry that is conducted with the expectation that the method, results, and conclusions will be able to withstand the scrutiny of the relevant research community
            - Initially exploratory work DOES NOT fall under research; however, pilot studies (small “substudies”) do count
            - Human Participants: those individuals whose data, biological materials, or

responses to interventions, stimuli or questions by the researcher, are relevant to answering the research question(s)
        - Includes biological materials (cells, cadavers, reproductive cells)
        - Information from individuals for expertise (non personal info) do not count as human participant; however, may classify as research participants
- Research exempt of REB review:
    - Uses info legally/publicly accessible with no expectation of privacy
    - Observes people in public spaces
        - No direct intervention staged by the researcher
        - No targeted groups for observation that also does not expect revealing anything private
    - Secondary use of anonymous information/human biological materials
        - Secondary use: info collected for a purpose other than what the current research purpose is
        - The information may not be associated with anyone or could not be identifiable with a person
- Activities exempt of REB review:
    - Quality assurance/quality improvement/program evaluation/performance reviews (eg. public health surveillance)
    - Creative practice activities (eg. interactive art installment with audience participation)
    - Questions to consider:
        - Is the activity being mandated by an organization?
        - Is participation in the activity a condition of employment or training?
        - Are the results intended to advance the purpose of the mandating organization?
            - If so, are the results also intended for a research purpose?
- Dual purpose projects:
    - Some research projects involving creative practices may use the data for research purposes
    - If any research aspect is present within an activity normally exempt of research, REB review is necessary
- Balancing risk and benefit:
    - The potential benefits must outweigh all foreseeable risks
        - Benefits must positively affect the welfare of participants, their communities, and/or society through the advancement of knowledge
        - Benefits to the researchers are insignificant in balancing risk and benefit
        - Risk: the possibility of the occurrence of harm to participants or other individuals
            - Harm includes negative effects on individuals' welfare (social, behavioural, psychological, physical, economic, etc.)
    - Research-attributable risks
        - Prospective participants must be informed of the potential benefits and foreseeable risks of participating in the research
    - Minimal risk research:
        - Research in which the likelihood of harm (or significance) is no greater than can be encountered in everyday life
        - Determining if a project is minimal risk helps the REB decide the appropriate level of review required for a research protocol

        - Risks to researchers are also important, and if they could become a safety concern, the REB may raise concerns about the research project
- Consent: means by which individuals express their willingness to participate in research
    - Key elements:
        - Voluntary (no coercion)
            - Because participation is voluntary, their may also withdraw their consent at any time and without any reason
            - Ethical obligations towards the individuals who may be vulnerable are also important
        - Informed
            - Prospective participants must be fully aware throughout the entire process the risks and potential benefits of being involved in the research
                - Any questions must be answered
                - Research purpose, how the information will be collected, how the results may be disseminated, etc. must be revealed as well
            - It is also important that the prospective participants actually understand what the researchers are telling them (technical jargon could undermine informed consent)
        - Ongoing
            - As parts of the research come up, researchers should follow up on the consent
            - If aspects change, researchers are expected to follow up and make sure that consent is given for any of the changes
    - Other notes:
        - Consent precedes participation in research
        - Consent must be documented (sometimes legal documentation)
        - TCPS 2 also has conditions for individuals who lack decision-making capacity themselves
    - Special circumstances:
        - The TCPS 2 has strict conditions for circumstances where the requirements for formal consent influence the outcomes of research questions
        - Researchers must justify their need to be approved by the REB.
        - Often, consent is required for the use of secondary information
            - Exceptions:
                - Identifiable information is essential for the research
                - The information is unlikely to adversely affect the individuals
                - Impossible/impracticable to seek consent
                - Researchers have obtained any other necessary permissions to use the information
        - Incidental finding: a discovery about research participants or prospective participants that is made in the course of research, but is outside the objectives of the research study
            - Likelihood of discovering an incidental finding must be presented during the consent process
- Fairness and equity:
    - No group should bear an unfair share of burdens in participating in research
    - Selection of participants is based on inclusion and exclusion criteria set by

the researchers
        - These should be directly related to the goals of the research, but can affect the fair and equitable distribution of burdens
        - **Including or excluding individuals for reasons unrelated to the research goes against the principle of justice, and can compromise the reliability and usefulness of research results**
    - Appropriate inclusion/inappropriate exclusion:
        - Convenience is <u>not</u> an appropriate reason to include/exclude a specific population
        - Exclusion criteria not justified by the research question violates the principle of Justice
            - Can delay and undermine the advancement of knowledge
            - Also just unethical
        - Exclusion of women, children, elderly, etc. who lack the capacity to consent may be excluded from research for reasons unrelated to the goals sometimes
            - However, exclusion of that demographic means that any research results cannot be reflect the realities of those groups
    - Vulnerability:
        - Can be caused by limited access to social goods, such as rights, opportunities, and power
        - It is necessary to include substitute decision-makers for vulnerable participants
    - Dissemination (spreading) of research results:
        - Is essential to the advancement of knowledge
        - Researchers are obligated to disseminate their results in a timely manner without restriction, regardless of whether or not the hypotheses are supported by the data.
- Privacy/Confidentiality:
    - Privacy: an individuals' right to be free from intrusion or interference of others
        - Includes an individual's body, personal information, expressed thoughts and opinions, personal communication with others, and the spaces they occupy
    - Confidentiality: the obligation of an individual or organization to safeguard entrusted information
        - Includes info about human biological materials
        - Federal, provincial, and/or territorial legislation may also protect privacy rights
        - **Part of confidentiality is researchers letting participants know what information they will be collecting, who will have access to it, how it will be protected, and how it will be used (related to consent).**
        - REBs share responsibility in ensuring that confidentiality is maintained
            - Measures include:
                - Type of info being collected
                - Purpose of collecting the information
                - How the information will be used
                - Limitations on the use, disclosure, and retention of the info
                - Risks to participants of data is breached
                - Security safeguards in place

            - Recordings of observations
            - Anticipated uses of the information
            - Any anticipated linkages in data between patients or other actors
        - Confidentiality is to be maintained through the institutions and organizations where the research data is being conducted/stored
    - Identifiable and non-identifiable information need to be distinguishable for the context of the research project
    - Info categories:
        - Directly identifying information: info directly associated with an individual
        - Indirectly identifying information: info that can be reasonably expected to identity with an individual through indirect identifiers
        - Coded information: information where any direct identifiers are removed and replaced with code, in which the code could potentially be used to re-identify the individual
        - Anonymized information: information that has direct identifiers permanently removed with no way of associating certain data with an individual
        - Anonymous information: information that never had identifiers associated with it anyways
- Conflicts of interest
    - Conflict of interest: an incompatibility of two or more duties, responsibilities or interests of an individual or institution as they relate to the ethical conduct of research, such that one cannot be fulfilled without compromising another
        - Could be commercial, financial, personal, professional
    - Types:
        - Real conflict: two duties/responsibilities/interests are indisputably contradictory
        - Potential conflict: doesn't presently exist but can be foreseen to occur
        - Perceived conflict: a conflict that may be seen through the eyes of external observers
    - Conflicts of interest can **undermine the integrity and legitimacy of the research process and impact the verity of the results**
    - Institutions:
        - Eg. raising funds may conflict with conditions that a donor has about how the
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        - data is shared
        - These institutions must have policies to help address conflicts of interest
        - Research conflicts of interest must be reported to the REB
        - REB individuals directly involved in the conflict of interest should not participate or vote in any discussions/situations that relate to

that conflict of interest
        - All researchers with conflicts of interest are responsible for declaring all types of financial incentives and benefits (conflicts of interest) they receive from the research in their application (REB will review it)
    - Avoiding conflicts of interest:
        - It begins by foreseeing and avoiding areas of potential conflict
        - When they exist, it is important to declare them (it causes more problems if conflicts arise after research has begun)
- REB Review:
    - REB: a body established by an institution to provide ethics oversight for research projects that involve human participants
        - REBs review project proposals to determine whether its ethics are acceptable or not
        - REBs also review the research on an ongoing basis
        - Ethical issues that arise through the course of the research must be reported to the REB (any intentional changes must also be reported to the REB)
    - Ethics review is distinct from scientific review (does not critique design, methods, etc.)
    - How REBs function:
        - They are impartial and not associated with other groups (ie. funding) related to an institution
        - They generally operate by consensus
        - REB reviews start by looking at the level of review (reviews must be proportionate to the level of risk)
    - REB demographic:
        - At least five members including two members with expertise in the area of research under review, a knowledgeable ethics member, a knowledgeable law member, and a community member (community member represents the perspective of a prospective participant). Generally, ethnic and social diversity is important.
            - REB administrators may need to participate in discussion, but they do not vote
            - REB members are obligated to disclose conflicts of interest
            - Generally, senior institutional administrators should not be involved in the REB decision-making process
    - Communication:
        - Questions should be addressed and resolved when communication is open
        - Decisions need to be communicated in an efficient and timely manner (decisions must be supported by reasons)
        - Appealing REB decisions is permitted if researchers and the REB are unable to resolve disagreements through deliberation
    - REB accountability:
        - The institutions that create the REB remain accountable for REB activity
            - Institution still oversees REB functions, such as the appointment of members and overall consideration if the REB is effectively carrying out its functions
        -
    - Multi-jurisdictional research
        - Under this circumstance, multiple institutions' REBs must agree on an appropriate model for review

        - If the research is minimal risk, the institutions can approve a single REB review without entering official agreements with each other
        - For Canadian research, REB review is necessary at both the Canadian institution and other bodies required if the site is outside of Canada.
    - Publicly declared emergencies
        - Policies should be in place to prepare for this rare situation.
        - Exceptions or infringements of ethics principles and REB procedures must be adequately justified, if necessary
- Indigenous Participants (this guidance can apply to non-Indigenous communities):
    - In the past, indigenous populations were not meaningfully engaged in research
    - Community: a group of people with a shared identity or interest that has the capacity to act or express itself as a collective
        - It is <u>imperative</u> that research is respectful of the customs and codes of indigenous communities
    - Community engagement, if necessary for the research, must respect and understand the priorities of the community, which may have conflicts of interest.
        - Eg. indigenous peoples make up a sizeable proportion of the study or community
    - Engagement may include meeting formally with community members, consulting with Elders, formally negotiating a research agreement, etc.
        - REBs need evidence of community engagement to receive ethical approval
    - Communities will decide to what extent they will be involved within the research
        - Some groups will want to collaborate in all stage of the research project, even having a leadership role
    - Formal research agreements may be necessary if the research aims to genuinely and fully collaborate with First Nations, Inuit, or Métis.
        - All other practices for gaining ethics approval still stay in place
    - Research agreements:
        - If research agreements are successful, terms and undertakings of both parties need to be clarified
        - With intellectual property, there is a joint responsibility for researchers/institutions to properly establish what is intellectual property and its significance within a study and its research agreement
    - Community capacity building:
        - With more indigenous communities wanting to participate in research, it is important to establish what level of capacity building is desired by the communities, so asking them is important

Ethics Course:
CITI Canada GCP (Oct. 20-29) CITI - Collaborative Institutional Tr...)

- Summary:
    - The GCP sets the standards for clinical research (among other things).
        - They make sure that patients will be protected and that the research is accurate and reliable.
    - In the past, research was reconducted for reliable use within countries, which was incredibly inconvenient.
        - So, in the early 1990s, the EU, Japan and US created the International Conference for Harmonization (ICH) to standardize regulations for clinical research, drug prescription/standards/marketing, etc.
        - In 2016, the ICH E6 GCP made modifications to clinical research standards in order to improve efficiency (they also renamed themselves the International Council for Harmonization).
        - These modifications were added under “Integrated Addendum To ICH E6(R1): Guidelines for Good Clinical Practice E6(R2)”.
    - Role of GCP:
        - The full name of the ICH is: International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
            - Founding members:
                - US FDA
                - European Commission
                - EFPIA
                - Ministry of Health and Welfare (Japan)
                - Japan Pharmaceuticals Manufacturers Association
                - PhRMA
            - Original Observers:
                - Health Canada
                - WHO
        - The ICH is governed by a steering committee and is supported by the ICH Secretariat (Secretariat is supported by the IFPMA)
        - The ICH has developed over 60 guidelines on:
            - Quality:
                - Relates to pharmaceutical and chemical quality assurances (for drugs)
            - Safety:
                - Relating to in vivo and in vitro pre medical procedures
                    - In vivo: procedure in the patient
                    - In vitro: procedure outside the patient (ie. in a test tube)
            - Efficacy:
                - Relating to research with human subjects
                - Includes the E6 GCP
            - Multidisciplinary:
                - Medical Terminology
                - Electronic Standards
                - Timing Pre-Clinical Trials to Clinical Trials
                - The Common Technical Document (CTD)
                - Data Elements and Standards for Drug Dictionaries
        - E6 GCP:
            - E refers to Efficacy
            - Pertains specifically to conduct of clinical research with human subjects with

relation to drug usage

- Good Clinical Practice (GCP): “A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.”
- Goals of the E6 GCP:
    - Assure that the rights, wellbeing and confidentiality of study participants is protected
    - Assure that study data is reliable and credible
- Health Canada originally adopted the E6 guidelines in 1997, in both English and French.
    - But Health Canada officially adopted the GCP in April 2019.
- ICH E6 GCP Guideline Sections:
    - Intro: describes the purpose of GCP as an international standard for the conduct of clinical research
    - Section 1: Glossary:
        - Includes a comprehensive glossary of terms used in the Guidelines and are integral to clinical research
    - Section 2: The Principles of ICH E6 GCP:
        - Describes the objectives of establishing international ethical principles and quality standards for clinical research, specifically for studies that support marketing applications (the predominant theme is protecting human subjects)
        - Principles:
            - Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirements.
            - Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trail participant and society. A trial should be initiated and continued only if the anticipated benefits justify the risk.
            - The rights, safety, and wellbeing of the trial participants are the most important considerations and should prevail over interests of science and society.
            - The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
            - Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
            - A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB/ interdependent ethics committee(IEC) approval/favorable opinion.
            - The medical care given to, and medical decisions made on behalf of, participants should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

        - Each individual involved in conducting a trial should be qualified by education, traising, and experience to perform their respective task(s).
        - Freely given informed consent should be obtained from every participant prior to clinical trial participation.
        - All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification. This principle applies to all records referenced in this guideline, irrespective of the type of media used.
        - The confidentiality of records that could identify participants should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements.
        - Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.
        - Systems with procedures that assure the quality of every aspect of the trial should be implemented. Aspects of the trial that are essential to ensure human participant protection and reliability of trial results should be the focus of such systems.
- Section 3: Institutional Review Board/Independent Ethics Committee (IRB/IEC):
    - REBs are review boards that oversee research involving human participants to assure the protection of their rights, safety and welfare.
- Section 4: Investigator
    - This section covers the role of the investigator regarding qualifications, resources, medical care of research participants, interactions with REBs, compliance with protocols, management of investigational products, informed consent of participants, recordkeeping, and reporting. All investigators must comply under ICH standards.
    - Investigator: a person responsible for the conduct of the clinical trial at a trial site. If a group of individuals is conducting the trials, the investigator would be the "leader" of the team, and would be called the principal investigator.
- Section 5: Sponsor:
    - Sponsors have standards that they must comply with. This section covers them.
    - The ICH recommends a quality management system that uses a risk-based approach.
- Section 6: Clinical Trial Protocol and Protocol Amendment(s):
    - Section includes the specific content standards for clinical trial protocols (trial design).
        - Includes all the topics that need to be covered in

the protocol
        - Section 7: Investigator's Brochure (IB)
        - Section 8: Essential Documents for the Conduct of a Clinical Trial
            - When documents are necessary to permit evaluation of a trial, this section summarizes the requirements for those documents, the purpose of the documents, and parties responsible for dealing with the records.
    - Other documents within the ICH documents that are important for clinical research include:
        - ICH E2A, Clinical Safety Data Management: Definitions and Standards for Expedited Reporting
        - ICH E8, General Considerations for Clinical Studies
    - **The ICH E6 GCP Guideline applies to all studies that will be submitted to Health Canada, and other regulatory agencies outside the US in support of marketing applications.**
    - Other drug studies are still expected to consider the GCP, although other policies may take precedence (eg. the Canadian Food and Drug Regulations)
        - Although generally, the ICH regulations are more specific and provide the most optimal conditions for trial execution. While these regulations do not contradict US FDA regulations, there are regulations in Canada that take precedence over the GCP.
            - Because the US FDA is well aligned with the GCP, they are guidance for FDA-regulated drug studies.
- Role of REBs:
    - AKA institutional review board (IRB) or independent ethics committee (IEC)
    - Role is to <u>ensure the protection of the rights and welfare of human participants in clinical trials.</u>
    - In Canada, REBs ensure that regulations such as the TCPS2 and GCP are followed
    - TCPS2 relates to all research involving human participants, while the GCP applies to clinical drug trials specifically
    - REB responsibilities:
        - They approve, reject, propose modifications to, monitor, suspend, and/or terminate ongoing research involving human participants for their protection
        - Done so by evaluation:
            - Quality of study proposal
            - Risk to participants
            - Consent of participants
            - Investigator qualifications
            - Participant compensation plans
        - They **continuously** review experiments
        - After reviewing a proposed study, they are responsible for providing either:
            - Approval
            - Any modifications required
            - Disapproval
            - Termination/Suspension
            - May request more info before making a decision
        - Special Circumstances:
            - Special attention is required for studies with vulnerable individuals (eg. cannot provide their own consent)
            - Non-therapeutic studies (no benefit to participant) must address adequately any ethical concerns
        - **Must follow written standard operating procedures and comply with the GCP**

- REB Composition:
    - At least five members
    - 1 member: primary area of interest NOT in science
    - 1 member: independent of the study
    - **Only REB members independent of the investigator/sponsor may vote**
    - Variation:
        - GCP:
            - As listed above
        - TCPS2:
            - At least five members
            - Men and women
            - 2 members with expertise in the area
            - 1 member knowledgeable in law
            - 1 member knowledgeable in ethics
            - 1 member with no affiliation to the institution
    - Operations:
        - Should be operated to avoid bias
        - Review should be timely, independent, and competent
        - Make decisions when there is a majority (preferably a consensus)
        - Implement systems for safety in study assessments
        - May invite nonmembers for consultants
        - ONLY members participating in the reviews may vote
        - May have the investigator provide additional information about the study, but cannot vote or participate in deliberations
- Ethics Review Procedure:
    - Determine composition (members of the review committee)
    - Schedule and notify members of meetings
    - Conduct an initial review of the studies
    - Determine frequency of continuing reviews
    - Provide additional requirements
    - Specify that no participants may be enrolled until ethics is approved
    - Specify that no deviations from the approved protocol can occur without an additional review by the REB
    - Specify that the investigator must report to REBs for deviations, changes in risk to participants, adverse drug reactions, or new information within the study
    - **REBs should promptly respond to investigators**
- Documents required for review:
    - Study protocol
    - Written consent forms
    - Investigator's brochure
    - Safety info
    - Info about payments for participants
    - Investigator's current curriculum vitae/other qualifying documents
    - Other documents
- **REBs should retain any relevant records from the reviews for a minimum of 3 years after the completion of a study**

- Sponsor Responsibilities:
    - ICH E6 GCP Section 5 outlines the roles and responsibilities for sponsors in clinical research.
    - Research teams must understand this in order to properly comply with the GCP and applicable regulations.
    - Who can be a sponsor:
        - Frequently are pharmaceutical companies, but can also be an individual,

academic institution, private organization, etc.
    - **"Sponsor" is not synonymous with "Funder"**
- GCP Definitions:
    - Sponsor: "an individual, company, institution, or organization which takes responsibility of the initiation, management, and/or financing of a clinical trial"
    - Sponsor-Investigator: "an individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (eg. doesn't include corporations or agencies). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator."
- Health Canada Definitions:
    - Sponsor: "an individual, corporate body, institution, or organization that conducts a clinical trial as per Division 5. The sponsor must comply with its obligations as set out in the Regulations (including C.05.10-C.05.015) in adhering to good clinical practices for the proper use of the drugs, drug labeling requirements, record keeping, submission of information, reporting of Adverse Drug Reactions (ADRs), and trial discontinuation reporting requirements."
- Sponsor responsibilities:
    - Quality management:
        - They are responsible for implementing a system to manage quality throughout the study process.
            - Quality management includes efficient design of protocols, data collection tools and procedures, and info for decision making.
        - Risk-based approach should be proportionate to the risk of the study if the study will impact participant safety and data integrity
            - Includes:
                - Critical process and data identification
                - Risk identification (system, protocol)
                - Risk evaluation (likelihood, impact, detection)
                - Risk control
                - Risk communication (including documentation)
                - Risk review
                - Risk reporting
    - Quality Assurance/Control:
        - Responsible for:
            - Implementing quality assurance/control systems
                - Includes standard operating procedures (SOPs)
                - SOPs:
                    - May be study or site specific
                    - Requires a process for approval and revisions
                    - Critical procedures should include:
                        - Informed consent process
                        - Adverse event management
                        - Study personnel training
                        - Investigational product management
                        - Record retention
                        - Biological specimen

management
- Equipment calibration
- Monitoring
- Securing written agreement for all involved parties
- Ensuring procedures are in place for handling data and ensuring reliability

- Contract Research Organization (CRO):
  - A sponsor may transfer some of its duties to a CRO, but needs to be documented.
    - The sponsor should ensure oversight of trial-related duties, even if managed by a CRO. **Responsibility for the quality and integrity of a study always resides with the sponsor.**
  - CROs should also have quality assurance processes.
- Medical Expertise:
  - The sponsor should designate qualified medical personnel to advise on study-related medical questions/problems.
  - Often referred to as medical monitors.
- Trial Design:
  - The sponsor should utilized qualified personnel throughout the entire study to oversee trial design (designing protocol and case report forms (CRFs), planning how to analyze the data, etc.)
- Trial Management, Data Handling, and Record Keeping:
  - Sponsors are responsible for the management of the study including data and record management. Expectations should be documented in written agreements.
    - Includes:
      - Source documents should be defined and how they are maintained needs to be clarified
      - Establishing an independent data monitoring committee (IIDMC) or data safety monitoring board (DSMB)
      - When using electronic data capture (EDC) systems, risk assessments, maintaining SOPs, maintaining security systems, maintaining a list of individuals, maintaining backups, and ensuring integrity of the data is necessary
- Investigator selection:
  - One key sponsor responsibility is to select investigators who have sufficient resources to properly conduct the study.
    - They should have curricula vitaes (CVs), medical licenses, and training certificates to provide if necessary
  - The sponsor should provide the investigators with necessary information to conduct the study.
- Allocation of Responsibilities:
  - The sponsor needs to outline, establish, and allocate all study-related duties, responsibilities, roles, etc.
- Compensation for Participants and Investigators:
  - In the event of a study-related injury or death, compensation and indemnity should be documented
- Financing:
  - Financial aspects of the study need to be documented
- Notifications to Regulatory Authorities:
  - A clinical trial application and any amendments need to be

submitted by the sponsors for review and approval (to any regulatory authorities)

- Confirmation of Review by REB:
    - The sponsor needs to ensure that all necessary ethics reviews and approvals are obtained (documented).
    - Sponsor needs to obtain:
        - The name and address of the REB
        - The statement from the REB that complies with the GCP
- Investigational Products (IPs) (frequently drugs/vaccines):
    - GCP standards require specific management of IPs
    - Sponsors should ensure not only that there is sufficient trial data to support the use of an IP, but that updates to the IB are made with any new significant information.
        - It should be done in a timely manner, and then sent to the applicable REB for review and approval.
    - If a sponsor is an academic investigator, they will not be responsible for updates to the IB, but will be responsible for obtaining materials required for REB review.
    - Sponsors should ensure that investigational products are manufactured in accordance with the Good Manufacturing Practices (GMP) and are coded and labeled in a manner that protects the blinding, and complies with labeling requirements.
    - The sponsor:
        - Provides the investigator with the IP along with information for safe use of the product
            - Ensures that REBs have approved them
            - IP is properly stored and instructions are available
        - Ensures IP compliance with labeling, reporting, and recordkeeping requirements
        - Maintains a system for the disposition of unused IPs
- Record Access:
    - Direct access to source data and documents for study-related monitoring, audits, REB review, and regulatory inspection must be ensured and specified in a protocol or other written agreement.
    - Participants' medical records and their informed consent should also be available.
- Safety Info and Adverse Drug Reaction Reporting:
    - Sponsor is responsible for:
        - Ongoing IP safety evaluation
        - Informing investigators and authorities of findings of
            - Something that could adversely affect the safety of research participants
            - Something that could impact the conduct of the study
            - Something that could impact the decision of an REBs approval to continue a study
        - Safety management and reporting of adverse events
            - Ongoing safety evaluations of IP
            - Setting up DSMB
            - Sending reports of all serious or unexpected adverse drug reactions to investigators and regulatory authorities as they come up
            - Preparing periodic safety updates for review by

regulatory authorities

- Monitoring:
    - Monitoring is an essential component to ensure quality by a Sponsor.
    - Purpose is to verify that:
        - Rights and wellbeing of research participants are protected
        - Study data is accurate, complete, and verifiable by source documents
        - The study is conducted in compliance with the currently approved protocol with amendments, with the GCP and other regulatory requirements.
    - Sponsor needs to ensure that the approach to monitoring is efficient and effective, using a systematic (risk-based if necessary) approach.
- Auditing:
    - A sponsor may conduct an audit to evaluate study conduct and compliance with protocol, SOPs, GCP, etc.
    - Auditing is independent of other processes (i.e. monitoring)
- Non-compliance:
    - Non-compliance with protocols should lead to prompt action by the sponsor to ensure compliance.
    - If non-compliance significantly impacts the participants' safety or data, corrective action preventative action plans (CAPAs) need to be implemented.
    - The sponsor should also consider other actions (termination of the study, etc.)
- Premature termination or suspension of a trial
    - If a study is prematurely terminated/suspended, the sponsor should inform the investigators promptly, along with the regulatory authorities. **A reason must be provided.**
    - The sponsor should also inform REBs and provide them with the information relating to it.
- Clinical Trial/Study Report:
    - Once a study is completed or terminated, the sponsor has the responsibility to ensure that study reports are prepared and provided as required by the standards of regulatory authorities.
- Multicentre Trials: a study that takes place in more than one location, but is operational under the same protocol
    - Ex. They may take place in one region at multiple institutions. Or on a national level across multiple cities.
    - Challenges of Multicentre/International Studies:
        - Complexity of study design
            - Studies are typically more complex than single site studies → higher costs
            - Adequate training must be ensured (conference/video calls may be necessary)
            - Protocol standardization is necessary, especially when practice varies between locations (provinces, countries)
            - Safety evaluations of IPs must meet the criteria for all applicable regulatory authorities
        - Authorship and credit:
            - Best to work out authorship in advance, because

it is hard to distribute credit with such a large team
- Quality control:
  - Maintaining a high standard across all sites can be challenging
    - Training standards must be high
    - Site monitoring must be diligent
    - ALL SITES must understand GCP requirements
  - Data completion:
    - Regulation communication between sites is imperative
- Ethical issues:
  - Submissions to all REBs can be annoying → a centralized submission process would be beneficial for resolving this
- Time constraints/time differences
- Funding
  - These projects can be quite costly
- Appropriate agreements must be in place prior to the study
- Cultural norms differ between countries, which may impact recruitment and thus, the reliability of data in drawing conclusions about certain populations (AP stats!)

- To solve these problems:
  - The study must be appropriately conducted
  - Participants' rights, safety, welfare, etc. must be protected throughout the entire study
  - Data collection must be accurate and reliable and consistent
- ***Communication is important for when unexpected problems arise (which they always do)

- Investigator-initiated studies where the investigator is also the sponsor
  - If an investigator is the sponsor, they are still held to the same standards as an external sponsor.
  - They are managed by the same regulations.
  - The sponsor/investigator is responsible for:
    - Study design
    - REB/committee approvals
    - Study conduct
    - Analysis and interpretation of results
    - Communication of results (eg. publication)
  - Challenges:
    - Understanding and dealing with all obligations and resources required can be challenging
    - Cannot miss any of the below:
      - Regulatory requirements
      - Funding/budgeting
      - Reporting
      - IP accountability
      - Agreements, insurance, liability
      - Ongoing safety evaluations
      - Quality assurance
      - Multicentre/international study (if applicable)

        - Burdens are almost always increased for sponsor-investigators.
- Investigator Responsibilities and GCP:
    - The investigator is responsible for the overall conduct of the study at the site (including protecting the rights and welfare of human participants, and maintaining the validity and integrity of data collected)
    - They must meet ALL applicable regulatory GCP, REB, sponsor, and institutional requirements.
    - Different definition:
        - GCP:
            - Investigator: “A Person responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.”
            - Sub-investigator: “Any individual member of the clinical study team designated and supervised by the investigator at a study site to perform clinical study-related procedures and/or to make important study-related decisions (associate, residents, research fellows).”
        - Health Canada:
            - Qualified Investigator (QI): “Person responsible to the sponsor for the conduct of a clinical trial at a clinical study site who is entitled to provide health care under the laws of the province where that clinical study site is located, and who is:
                - In the case of a clinical trial respecting a drug to be used for dental purposes only, a physician or dentist and a member in good standing of a professional medical or dental association.
                - In any other case, a physician and member in good standing of a professional medical association”
        - US FDA:
            - Clinical Investigator: “An individual(s) who actually conducts a clinical investigation (that is, under whose immediate direction the drug or biologic is administered or dispensed to a subject)”
    - Investigator Qualifications:
        - Must demonstrate that they have the education, training, and experience to conduct the study.
        - Must demonstrate their awareness of GCP and other regulatory requirements.
        - Is required to be familiar with the protocol, IB, and other investigational products
        - ALL members that are delegated study-related tasks/duties must also be qualified, competent, and trained. THIS IS REALLY IMPORTANT.
        - If involved, external individuals, institutional support services, or third parties must also be qualified.
        - The investigator is responsible for ensuring that all staff who are involved are:
            - Adequately informed and familiar with the study and protocol
                - Especially the specific details and investigational products that are required
            - Are aware of regulatory requirements, GCP, acceptable standards, etc.
            - Are informed of any pertinent change during the conduct of an experiment, and receive additional training if necessary
    - **Investigators can delegate tasks to others, but they always remain responsible for**

the study.

- They must supervise all tasks and maintain those tasks in the Delegation Log, or Delegation of Authority Log (DoA log).
    - The delegation log should document who was involved, their qualifications, when they were involved, and what their study duties were. Evidence of training for the delegated tasks is required.
    - The delegation log should be constantly reviewed and updated throughout the study.
    - Evidence of qualifications should be maintained and updated.
- The investigator should permit inspections by regulatory authorities when required.

- Required investigator resources:
    - Suitable research participants - ability to meet requirements set out in the protocol
    - Time - enough time to conduct, superise, and complete the study
    - Facilities and qualified study members
    - Tip: study sponsors often choose to work with investigators who have consistently met their projected study timelines, etc.
- Medical Care of Research Participants:
    - Investigator is responsible for:
        - Ensuring that trial related medical decisions are made only by qualified physicians
        - Treating research participants in the event of an emergency
        - Informing research participants when medical care is necessary
        - Removing research participants from the study if necessary
        - Informing the research participant's' primary physician about their participation in the study
        - Determine why research participants have decided to withdraw from the study, if possible
- Communication with REBs:
    - IEC: An independent body (a review board or a committee, institutional, regional national, or supranational), constituted of medical professionals and non-medical members, whose responsibility is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favourable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects.
    - IRB: An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is the ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.
    - REB approval is necessary before starting a study, and the investigator is responsible for submitting documents, including the study protocol, to the REB
        - Documents include:
            - Study protocol
            - Written informed consent forms and updates
            - Recruitment procedures and advertisements
            - Information provided to research participants

        - Other required reportings:
            - New info that could adversely affect the safety of participants
            - Unexpected serious adverse events, as per REB SOPs
            - Changes increasing the risk to research participants
            - Protocol Deviations
- Compliance with the protocol:
    - A well-written and planned protocol is the basis for a GCP complaint study
    - The protocol:
        - Describes the objectives, design, methodology, statistical considerations, and organization of a clinical research study
        - Provides the basis for ethical and scientific review, including study monitoring and the overall conduct of the study
    - Compliance with the protocol means performing all the study activities in a precise manner specified in the REB-approved protocol.
    - Revisions/additions/deletions must be resubmitted to the REB for review
        - The investigator is responsible for this.
        - The investigator should not implement any deviation from, or changes to the protocol without agreement by the sponsor and prior review and documented approval from the REB is received.
            - EXCEPTION: the deviation is necessary to eliminate an immediate hazard to research participants, or when the changes involve only logistical or administrative aspects of the study
        - In Canada, Health Canada also needs to authorize any changes.
        - All deviations must be documented and submitted to the REB
    - The investigator should sign the protocol
        - Once again, the protocol MUST BE FOLLOWED.
- GCP Guidance for Protocol Sections:
    - General Info
    - Background Info
    - Trial Objectives/Purposes
    - Trial Design
    - Selection and Withdrawal of Subjects
    - Treatment of Subjects
    - Assessment of Efficacy
    - Assessment of Safety
    - Statistics
    - Direct Access to Source Data/Documents
    - Quality Control and Quality Assurance Procedures
    - Ethics
    - Data Handling and REcord Keeping
    - Financing and Insurance
    - Publication Policy
    - Supplements
- Investigational Products
    - The investigator is responsible for the management, storage, security, and administration of the investigational products.
    - Records need to be maintained for:
        - Product delivery and temperature
        - Product inventory
        - Product use by each research participant as per protocol
        - Product storage requirements and status
        - Return and reconciliation of the product to sponsors or disposition

of unused products
        - Product record:
            - Date, quantity, batch/serial number, expiration date, unique code numbers, etc.
    - Investigational products should only be used in accordance with the approved protocol.
- Randomization procedures and unblinding
    - Randomization aims to assign participants to different study arms without bias.
        - Double-blinded treatments are even more effective (neither the investigator or the study participant knows which study arm the participant is being assigned.
        - However, the code must be protected/secured from accidental unblinding, but must also be accessible 24 hours a day at the study site in the event of an emergency.
        - Emergencies:
            - The investigator may need to know which study treatment a research participant is receiving.
            - If so, the investigator should follow unblinding procedures in the protocol.
            - The investigator must document and explain to the sponsor and REBs the reason for unblinding. This should be documented, including the reason the code was broken, who did it, and when.
- Informed consent of research participants
    - Informed consent MUST be obtained before ANY study-related procedures are undertaken that impact the participants.
    - Apart from consent, participants should also receive specific information about the study, including the purpose, duration, risks, benefits, costs, expenses, procedures, etc.
    - Some REBs may have rules about informed consent.
    - Consent is a process, and participants should be asked about informed consent whenever they are involved in the research.
- Records/Reports:
    - The investigator is responsible for maintaining adequate and accurate source documents, trial records, observations, and other data pertinent to the study for each research participant.
    - Source notes: an essential document required by GCP guidelines which is defined as any document in which information, an observation or data generated relevant to the study, is recorded for the first time
        - Source data: all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of data.
    - Good documentation practices is IMPERATIVE
        - They also help facilitate proper evaluation and validation of the study.
    - All studies must maintain essential documents.
        - Essential documents: documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced
            - Essential documents are to be generated before the clinical phase of a trail, and then updated during the trial and after the completion/termination of the trial

- Record retention requirements:
    - Essential documents must be retained until at least 2 years after the last approval of a marketing application in an ICH region, and until there are no pending or contemplated marketing applications in an ICH region, or at least 2 years have elapsed since the formal discontinuation of a clinical development of the investigational product.
    - In Canada:
        - Health Canada has regulated that for research, the original records need to be kept 15 years from study completion. Sponsors also need to define what constitutes study completion, and set an appropriate records retention start date.
        - The sponsor has the responsibility to inform the investigator to see when documents no longer need to be retained.
    - In US (FDA):
        - Investigators must maintain study records for at least 2 years
- Progress Reports/Final Reports:
    - Investigators need to be aware of regulatory, sponsor, REB, and institutional requirements for the submission of progress reports.
    - The reports should be written, and should highlight any significant changes affecting the study or increased risk to participants.
    - When studies have been completed, investigators must submit all their required reports to their institutions and sponsors.
        - Regulatory authorities should also be notified.
    - Note: REBs, institutions, and sponsors may have different policies for report submission and timelines
- Safety Reporting:
    - All adverse events (ADs) need to be appropriately identified, **documented, reported**, and managed.
    - Serious adverse events (SAEs) should be reported immediately to the sponsor, unless otherwise specified in the protocol.
    - Regulatory requirements must also be followed
- Premature Termination/Suspension of a Trial:
    - If a study is prematurely terminated, the investigator must promptly report that to their sponsor, REB, and if necessary, regulatory authorities.
    - Research participants must also be informed, and any appropriate therapy and follow-up must be provided.
    - If a study is terminated, the following is required:
        - Written information and explanation for REB and Sponsors if terminated by the investigator
        - Written information and explanation for REB and investigator if terminated by the sponsor
        - Written information and explanation for the sponsor and investigator if terminated by the REB

- Managing Investigational Products (Drugs):
    - Investigational drugs are not commercially available to consumers.
    - Definition:
        - Investigational product: a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled in a way

different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use

- Investigational new drug: a new drug, antibiotic drug, or biological drug that is used in a clinical investigation.
    - Includes a biological product that is used in vitro for diagnostic purposes
- Regulations of investigational products:
    - An investigational product cannot be shipped to a clinical site before regulatory approval in Canada (a no-objection letter)
        - Additionally, a completed Clinical Trial Site information form must be sent to Health Canada by the research sponsor.
        - Canadian Food and Drug Regulations:
            - A sponsor may sell or import a drug for the purposes of a clinical trial in respect of a new drug that has been issued a notice of compliance, if the clinical trial is in respect of a purpose or condition of use for which the notice of compliance is issued; or a drug, other than a new drug, that has been assigned a drug identification, if the clinical trial is in respect of a use or purpose for which the drug identification number was assigned.
    - In the US, the research sponsor must file an Investigational New Drug (IND) form or an Investigational Device Exemption (IDE) to the FDA.
        - The IND/IDE outlines the general investigational plan for the development of the drug or device.
        - Credentials of each investigator and sub investigator who will use the investigational product must be provided to the FDA.
        - Investigators must agree to:
            - Personally conduct or supervise the investigation according to the protocol
            - Inform the participants that the drugs are being used for investigational purposes (and other informed consent is received)
            - Maintain complete and accurate records and make records available for inspection of the use of investigational products
- Investigator control of investigational products:
    - **The legal responsibility for drug supply and handling is to the sponsor, who is obliged to ensure that the investigator is following the GCP.**
    - “Every sponsor shall ensure that a clinical trial is conducted in accordance with good clinical practices, and without limiting the generality of the foregoing, shall ensure that the clinical trial is scientifically sound and clearly described in a protocol; and the clinical trial is conducted, and the drug is used, in accordance with the protocol and this Division.”
    - “The sponsor is responsible for supplying the investigator(s)/institution(s) with the investigational product(s).”
    - “The sponsor should not supply an investigator/institution with the investigational product(s) until the sponsor obtains all required

documentation."
- **Responsibility of investigational products accountability at the trial site falls on the investigator.**
- US FDA:
    - "An investigator shall administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub investigator responsible to the investigator. The investigator shall not supply the investigational drug to any person not authorized under this part to receive it."
- GCP:
    - The investigator is responsible for product accountability at the study site and maintenance of the clinical and research records.
- Product accountability includes:
    - Receipt of the product at the site
    - Supplying the product to research participants
    - Monitoring usage by participants
    - Return/destruction of the product at the end of the trial
- **Investigators are responsible for every individual unit of the product received.**
    - However, investigators can delegate responsibility to qualified personnel, such as the pharmacist or study coordinator. However, the investigator remains responsible for them.

- Packaging of Investigational Products:
    - Randomization can be facilitated through product packaging. Typically, drug manufacturers will package the investigational drug according to the individual clinical trial needs.
    - Early phase clinical trials (Phase I):
        - Smaller quantities of drugs are needed.
        - Generally supplied in bulk containers (eg. bottles of 100 tablets)
    - Later phase clinical trials (Phase II):
        - Packaging becomes more specific to the clinical trial schema (eg. packaging and generating labels including info like participant number and randomized treatment)
        - This helps facilitate compliance with the randomization process.
    - Packaging Example: Blister Packages (drugs in a plastic dome on a card
        - Easy to use
        - Package one dose per dome
        - Carry specific written information of the card
        - Maintains blinding (frequently)
    - Drug Labeling in Canada:
        - In Canada, labels must be in English AND French
        - Labeling information must include:
            - Statement indicating that the drug is an investigational drug to be used only by a qualified investigator
            - Name, number, identifying mark of the drug
            - Expiration date of the drug
            - Recommended storage conditions for the drug

            - Lot number of the drug
            - Name and address of the sponsor
            - Protocol code or identification
            - If the drug is radiopharmaceutical
        - Drug Labeling in US:
            - Labeling information must include:
                - Name of the study
                - Name of the study drug (even if it is a placebo)
                - Subject study number
                - How it is supplied
                - Dose per unit
                - Lot number
                - Batch number
                - Federal statement limiting use to experimental studies (eg. “Caution: New Drug - Limited by Federal Law to Investigational Use”)
- Shipping of investigational products:
    - The sponsor must have submitted an application to the Minister, and have approved the necessary research ethics.
    - Supplies are then ordered and shipped according to sponsor policies/procedures AFTER all forms have been completed and approval has been granted.
    - The investigator is responsible for verifying that the package arrived intact and that the contents match the shipping invoice.
    - In the study protocol, a description of the physical appearance of the investigational product should be included.
    - To avoid delays, investigators must anticipate when additional supplies need to be ordered (they should be ordered well before they are actually needed (2-4+ weeks)
- Storage of investigational products:
    - Investigational products must be stored according to protocol specifications/manufacturer’s directions. (generally, storage requirements are in the study protocol)
    - Generally, the pharmacy is the best place to store investigational drug products.
    - The location being stored should be secure (only accessible to authorized personnel).
    - If a research pharmacy is not available, investigational products can be stored so long as the following requirements are met:
        - Sponsor-directed storage requirements are met
        - Area is monitored, with written evidence of appropriate storage conditions (eg. temperature/refrigeration)
        - Access is limited at all times (eg. key is necessary)
        - Product is supplied only to research participants
        - Accountability records are maintained
        - Space is adequate
        - Investigator is ultimately responsible for the investigational products
        - Failure to maintain the product can lead to inefficacy of the product, or disqualification of data
- Dispensing of investigational products:
    - Administration/dispensing of investigational products occurs under the supervision of the investigator/sub investigator.
    - Investigational products may only be dispensed to research

participants enrolled in the specific clinical trial.
    - Ways of administering the investigational products:
        - Directly to the research participant from the research pharmacy
        - Given to the study coordinator to dispense to the participants
        - Administered to participants
        - Given to the pharmacist to prepare for administration, particularly for intravenous formulations
    - **Check the expiration date of the drugs.**
    - When drugs are dispensed, the administrator must record the drug name, dosage, the participant's identification code, etc. on a drug accountability form.
        - Some sponsors, research pharmacies, and institutions closely track investigational products.
        - Information should also be tracked and noted on the research participant's medical record, to record the experimental product exposure.
        - This is all generally accomplished with a case report form (CRF).
- Managing investigational product use by research participants:
    - If drugs are directly administered to the patients, they have the same level of accountability that the investigators do. They are obligated to return all unused drugs to the site, so the sponsor can destroy them, or do something else with them.
    - The number of returned drugs must be counted and diligently documented, and can be used to measure participant compliance.
    - Communication is IMPERATIVE to ensure research compliance. Written directions and assessing participants for understanding may yield more reliable data and enhance participant safety.
- Unblinding and Randomization:
    - When studies are double-blinded, the packaging labels do not explicitly indicate whether the product is a placebo, active control, or investigational product, but instead have a code to correspond to a treatment.
    - **The code should be broken only when the identity of the investigational product that the research participant received will determine the treatment to be given to that participant for the emergency.**
    - Sometimes, the codes are generated and managed by the sponsors. This aims to minimize participant differences among the study arms.
    - **Individuals who evaluate participant outcomes should not have access to the randomization codes.**
    - If the randomization/blinding code is broken, the statistical significance of the study data can be diminished.
- Final disposition of investigational products:
    - All unused investigational products must be returned to the sponsor, or disposed of as per the sponsor's instructions.
        - Other forms of disposition must be explicitly authorized by the sponsor.
    - Frequently, sponsor representatives observe the destruction of the study product.
    - Drug usage is reconciled by reviewing the paper trail:

- Shipping records showing receipts
- Dispensing/administration records showing usage of the product
- Reconciliation records for unaccounted products
- Final disposition records

- Informed Consent:
  - Informed Consent: “a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form”
  - Informed Consent in Canada:
    - The requirements for informed consent in Canada is codified in Division 5 of Canada Food and Drug Regulations, specifically under Sponsor Obligations, GCP
    - Although the qualified investigator is responsible for performing the informed consent procedure, either personally, ro by delegation to a suitably qualified study team member, the **trial sponsor** retains the ultimate legal obligation to ensure that this is being performed correctly, and is compliant to all legal requirements.
    - “Every sponsor shall ensure that a clinical trial is conducted in accordance with good clinical practices…”
    - “[...] written informed consent, given in accordance with the applicable laws governing consent, is obtained from every person before that person participates in the clinical trial, but only after that person has been informed of the risks and anticipated benefits to his or her health arising from participation in the clinical trial, and all other aspects of the clinical trial that are necessary for that person to make the decision to participate in the clinical trial.
    - Informed consent process:
      - Involves educating prospective participants prior to any study involvement, and continues even after the participant has signed the consent form.
      - Any time there is a change to the study, informed consent is required.
        - Research participants have the right to withdraw from the study at any time, especially after being informed of any changes to the study.
      - Process:
        - Informed consent form (ICF):
          - All GCP elements are present
          - REB approved
          - Correct version
        - Comprehensive dialogue has been carried out, with questions and concerns addressed
        - Adequate time has been given to the participant to review the info
        - Research staff should assess the participant’s understanding by asking questions
        - Signatures
        - Reconsenting if necessary
        - Ongoing consent
      - Every encounter with a research participant provides an opportunity for verbal consent. Participants must understand what

is happening.
    - If the study changes, and the ICF needs to be revised, participants must re-consent and re-sign the ICF which is potentially updated with:
        - The increase in incidence of risk to participants
        - New risks identified
        - Identification of a previously unknown serious side effect.
        - Decrease in expected benefit
        - New standard of care alternatives
        - Changes to medical treatment
        - Change in drug dosage/device application
        - Change in duration of participation
        - Change in sample size
        - Change in the use of sample taken
- REB approvals:
    - Informed consent process and all written information must comply with GCP principles, and approval must be obtained from the REB before studies begin.
    - Any revisions to the ICF/accompanying materials must be reviewed and reapproved by the REB.
    - Researchers must be aware of the 'fine line' between clearly and fully explaining the trial. Coercion or incentives being offered should not influence the consent.
        - Thus, financial incentives must be disclosed to the REBs, to ensure that amounts are appropriate.
- ICF language:
    - ICF language should be easily understandable and nontechnical, and should be available for the first languages of all study participants (not just English and French).
        - If English or French is not the primary language, an impartial translator is required for all consent visits when English or French is not the primary language.
- ICF content:
    - Involves research
    - Research purpose
    - Treatment arms and randomization
    - Experimental aspects of the study
    - Description of all investigative procedures
    - Participant's responsibilities and time commitment
    - Duration of trial and proposed number of participants
    - Expected benefits and potential risks
    - Alternate treatments, if participant declines participation
    - Treatment or compensation for trial injuries
    - Participant expenses, reimbursements, etc.
    - Voluntariness
    - Revised information for re-consent
    - Ability to withdraw consent without prejudice for alternate treatment
    - Confidentiality of information and authorized access to records
    - Contact information for questions or reporting trial-related injuries
    - Please refer to your REB's guidelines
    - Etc.
- ICF copies and signatures:
    - Investigators should encourage the participant to have a family

member or friend present for the discussion before making the final decision.
        - The participant must personally sign and date the ICF if consenting to the research protocol.
        - The dated signature of the person conducting the discussion must also be included on the ICF.
        - Study participants should be given a copy of the signed ICF.
    - Impartial Witness:
        - For prospective participants who are unable to read, due to lack of education or existing medical conditions will need an impartial witness whenever written information is presented such as informed consent or updates.
        - The witness should indicate by the dated signature that the information was fully explained and understood and that the participant consented without coercion. A copy of the ICF may be given to the witness in addition to the participant.
    - Legally accepted representatives, minors, emergency consent, etc.:
        - Some individuals may be unable to provide written or oral consent. The participant should be informed to the extent of their understanding. If capable, the participant's dated signature should also be obtained, in addition to that of the legally acceptable representative.
        - A legally acceptable representative may provide written consent <u>in emergency situations</u>. If no representative is present, enrollment should only be done as described in the study protocol.
    - Vulnerable Participants:
        - Vulnerable Subject: "an individual whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, or benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent."
        - It is IMPERATIVE that we consider vulnerability and if there are sufficient safeguards in the research project to protect the rights and welfare of these individuals.
    - Non-therapeutic trials:
        - REB approval is still necessary; however, **only persons fully capable of providing personal consent should be required for the trial.**
            - However, sometimes, this is not possible; so, these studies may be permitted so long as they are low risk, and cannot be carried out with this group of participants.
- Informed Consent in the US:
    - Informed consent must include
        - Information that the study involves research:
            - An explanation of the purposes of the research
            - The expected duration of the participant's participation
            - Description of the procedures to be followed

        - Identification of any procedures that are experimental
    - Clear description of the risks or discomforts to the participant
        - Must be accurate and reasonable
        - Must review any risks related to procedures and tests relating solely to research
        - Inform the subject of previously reported adverse effects
    - Description of the benefits to the participants or to others
    - Disclosure of any alternative procedures or treatments that may be advantageous to the participant; thus, giving the participant a full range of available options.
    - Description explaining how the institution/investigator will maintain confidentiality of records (include full disclosure and description of approved agencies, such as the US FDA)
    - For medium-high risk research:
        - Whether there will be any compensation
        - Whether there will be any medical treatment offered, and who will bear the financial responsibility for treatment if injury occurs
        - Where the participant may obtain further information
    - The specific office, name, and telephone number(s) of whom to contact for further information
    - A statement that participation is voluntary, and that refusal to participate involves no penalty or loss of benefits to which the person was otherwise entitled to
    - The subject may discontinue at any time
- Other requirements:
    - A statement that the procedure may involve unforeseeable risks (potentially to pregnancy)
    - A description of circumstances under which the participant's participation may be terminated without consent
    - A description of any additional costs to the participant that may result from participation in the research
    - A clear statement of the consequences of a participant's decision to withdraw from the research, and how to do so SAFELY
    - A statement that significant new findings developed during research which may relate to the participant's willingness to continue will be provided to the participant
- US Regulatory Groups::
    - US FDA
    - Office for Human Research Protections
    - IRBs/REBs
- Obtaining informed consent:
    - Involves:
        - Providing information to the participant
        - Ensuring the participant understands by answering questions the participant may have
        - Obtaining the voluntary agreement of the participant to participate in the study
- Providing information:
    - Guidelines include:
        - Advertising cannot be coercive or make false promises or claims
        - The information must be communicated in a manner and language that is clear and understandable

- The information communicated should not use exculpatory language
- Procedures to screen potential participants for eligibility must protect the rights and welfare of the prospective participants
- Institutional IRB approval

- Ensuring understanding:
  - Guidelines include:
    - Providing consent in a language that is understandable
    - When an interpreter is used, a written IRB approved translation is required
    - Giving the person enough time to think about their research before consenting
- Obtaining Voluntary Agreement to Participate:
  - Informed consent shall be obtained:
    - From the participant/legally authorized representative
    - Under circumstances that provide the participant with an opportunity to consider whether or not the participate and that minimize coercive influences
    - In a manner that doesn't include any language through which the participant is made to waive or appear to waive any of his/her legal rights or any language that releases the investigator, sponsor, or institution from liability for negligence

- Special Challenges:
  - Cultural issues:
    - In circumstances where cultural issues conflict with consent, the question of who conducts the consent process and how it is explained becomes even more important.

- Detection, Evaluation, and Reporting of Adverse, and Serious Adverse Events
  - One objective of clinical research is to determine the safety of investigational products. The data can be critical to obtaining approval for marketing a new product.
  - However, events can occur during the trials that are serious and unexpected that may require attention and can affect the safety of the research participants.
  - Defining an Adverse/Serious Adverse Event:
    - GCP:
      - Adverse event: any untoward medical occurrence in a patient or clinical investigation participant given a pharmaceutical product; does not necessarily have a causal relationship with such treatment
      - Adverse drug reaction:
        - Before market approval: any noxious and unintended response to a medicinal product related to any dose; causal relationship between eh medicinal product and an AR is at least a reasonable possibility
        - After market approval: any noxious and unintended response to a product that occurs at doses normally used in humans to prevent, diagnose, or treat disease or to modify physiological function.
      - Serious adverse event (SAE): any untoward medical occurrence that at any dose:
        - Results in death
        - Is life threatening
        - Requires inpatient hospitalization or prolongation of existing hospitalization

            - Results in persistent or significant disability/incapacity
            - Is a congenital anomaly
            - Causes other medically significant events
        - Unexpected Adverse Event: an adverse reaction, the nature or severity of which is not consistent with the applicable product information (eg. IB)
        - NOTE: a medical event may be classified as a serious adverse drug experience if it may jeopardize the participant and may require medical or surgical intervention, even if it doesn't fulfill the criteria listed above
    - Other definitions:
        - Associated: a reasonable possibility that the event could have been caused by the product
        - Disability: a substantial disruption of a person's ability to conduct normal life functions
        - Life-threatening adverse drug experience: any adverse drug experience that places the subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, that is, it does not include reactions that, had they occurred in more severe forms, might have caused death
    - **Serious, unexpected adverse events must be reported to Health Canada and the FDA**.
- Identifying Adverse Events:
    - AEs can be directly observed by research staff or reported by research participants.
    - Examples:
        - A rash noted during a physical examination
        - A headache that the participant mentions during a study visit
    - **It is the responsibility of the site staff (with assistance from the sponsor if needed) to investigate, identify, and classify adverse events. <u>SPECIFICALLY, IT IS THE RESPONSIBILITY OF THE PRINCIPAL INVESTIGATOR TO ASSESS CAUSALITY.</u>**.
    - Subjective vs. Objective Data Collection:
        - Data from AEs can come from objective or subjective measures. Thus, it is important for the principal investigator and research staff to investigate further to evaluate the circumstances.
    - Change From Baseline:
        - A change from the baseline condition may constitute an AE.
        - Baseline: the point when the clinical research starts, before any research-related procedures or treatments have begun
        - Change-from-baseline AEs can take on 2 forms:
            - Appearance of a new symptom/sign
            - Increased severity or frequency of an existing symptom/sign
        - In this circumstance, the investigator should consider the possible relationship between the AE and the investigational product.
        - NOTE: the failure of an investigational product does not constitute an AE (the drug doesn't lessen symptoms)
    - Sources used to Identify AEs:
        - Participant diaries: participants may be asked to keep a diary recording signs and symptoms occurring between study visits
        - Direct observation: physical examinations
        - Participant reports: participants should be asked about events that occurred between study visits (eg. symptoms)

        - Laboratory reports: determined values/outcomes are different from what was expected
        - Other medical reports: second-hand observation, medical records/documents, etc.
- Treatment of Adverse Events: Protocol Directed and Standard of Care
    - When an AE is detected, treatment may be required. The treatment should be administered by a medically qualified individual
    - Often, protocol guidelines may anticipate certain reactions and can aid in treatment
        - Examples:
            - If a participant develops a rash, they should receive this type of therapy
            - If a participants' hormone count fall below this amount, the next dose should be reduced by this percent
    - If unblinding is necessary to treat an AE, the investigator is responsible for documenting and reporting this to the sponsor and REBs
- Determining severity:
    - Severity refers to the intensity of the event and is generally indicated as mild, moderate, or severe.
    - Metrics:
        - None: no signs/symptoms or is within normal limits
        - Minor: minor signs/symptoms, no specific medical intervention required; asymptomatic laboratory findings, only, radiographic findings only; marginal clinical relevance
        - Moderate: requiring minimal, local, or non-invasive intervention only
        - Severe: significant symptoms requiring hospitalization or invasive intervention
        - Life-threatening or disabling: complicated by acute, life-threatening metabolic or cardiovascular complications (such as circulatory failure, hemorrhage, sepsis); life-threatening physiological consequences; or need for intensive care or emergent invasive procedure
        - Fatal: causing death
    - Other metrics:
        - Mild: an awareness of symptoms but easily tolerated
        - Moderate: symptoms interfere with normal daily activities
        - Severe: symptoms are incapacitating, with the inability to perform daily activities
    - There is also the Common Terminology Criteria for Adverse Events (CTCAE) scale.
    - <u>Severe ≠ serious</u>
- Determining causality:
    - Causality refers to the likelihood and extent that the investigational product being studied contributed to the development of an AE and involves medical decision making and discretion.
    - The principal investigator who has medical expertise should be making the causality determination.
    - Reporting may be necessary if causality is determined.
    - Elimination of Other Causes:
        - Often, the adverse effects of a treatment versus a natural

disease are hard to distinguish.
        - Research participants may be receiving other treatments as well, which could have some impact.
        - It is important for the investigator to consider the drugs and supplements the participant is taking, in addition to diet and other environmental factors for determining the causality of an AE. This is known as "drug-drug interaction".
    - Known Effect of the Drug/Drug Class:
        - The IB and background or a protocol should delineate known effects of the investigational product, for which the investigators can refer to.
    - Temporal Sequence:
        - The timing of the AE also provides information relevant to determining the cause of the AE.
        - Therefore, it is important to know how the drug impacts the body and the timeframe that effects may arise.
    - Chronic Effects:
        - Some AEs may not appear until after the participant has received the treatment, or even further after (eg. after the treatment was discontinued).
        - Causal relationships between the investigational product and the AE is much more difficult to assess.
    - Cumulative Effects:
        - Sometimes, an AE occurs only after a certain dose level has been reached.
    - Late Effects:
        - Some events are not discerned until long after administration of the investigational product.
    - Rechallenge:
        - One method to determine causality is to discontinue the product to allow the event to resolve or stabilize, before reintroducing the product. If the AE recurs, it is highly likely that the AE is related to the investigational product.
- Categories of Causality:
    - Definitely related: there is certainty that the event is related to the investigational product
    - Probably related: there is a high likelihood that the event is related to the investigational product
    - Possible related: there is likelihood that the event is related to the investigational product
    - Unlikely to be related: it is not likely that the event is related to the investigational product (other causes are present)
    - Unrelated: evidence exists that the event is related to something other than the investigational product
    - GCP definitions:
        - Criteria:
            - Has a reasonable temporal relationship to the intervention
            - Could have have readily been produced by the participant's clinical state or have been due to environmental or other interventions
            - Follows a known pattern of response to intervention

- Disappears or decreases with reduction in dose or cessation of intervention and recurs with re-exposure
- Definite: four
- Probably: three
- Possible: two
- Unlikely: two of the below
  - Does not have a temporal relationship
  - Could have been produced by the participant's clinical state
  - Could have been due to environmental factors
  - Does not follow a known pattern of response to intervention
  - Does not reappear or worsen with reintroduction of intervention

- Duration of AEs:
  - It is also important to evaluate the duration of the event.
    - Onset of the event should be measured from the onset of signs and symptoms.
  - Some events continue or change in severity over time. Capturing this information is also important, and can be used to help determine causality.
    - This should all be documented.
- Recording and reporting AEs:
  - It is often necessary to distinguish between an AE and a sign of a symptom of a disease or condition being studied or already exists.
    - Frequently, research sponsors will create separate forms to capture this variation.
    - The information must be collected to determine whether differences in disease symptoms or progression of the disease might also be drug-related events.
  - Investigative sites are responsible for recording and reporting observations of AEs experienced by human participants during clinical research. Reports frequently become part of the product's profile.

- Reporting SAEs under CTA or IND:
  - When an AE meets the requirements for an SAE, and it is unexpected and associated with the investigational product, Health Canada and FDA require investigators to report the event to the sponsor in an expedited manner. This allows sponsors to assess all the SAEs and observe trends across investigative sites.
  - The sponsor and the investigator may disagree about the relatedness of the SAE to the investigational product. There aren't regulations on how to resolve the differences, so disagreements are most frequently just documented in reports.
  - Reporting by Investigators:
    - "Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol."
    - The industry standard is to report all SAEs within 24 hours of identification. If the event is life-threatening or fatal, the event should be reported immediately.
    - Expedited reporting if events are serious but expected, or not

reasonably related to the investigational product
        - These, however, may be prompted to be reported by the sponsors and REBs, according to local requirements.
    - Sponsors also typically require expanded reporting of SAEs vs. AEs. (additional forms may need to be completed)
    - Information to include in SAE reports
        - Demographic data (eg. sex, date of birth, height, weight, etc.)
        - Product information (eg. brand name, dosage form and strength, route of administration, etc.)
        - Other treatments
        - Details of the suspected adverse event (eg. timeframe, symptoms, etc.)
        - Treatment of event
        - Outcome
        - Details of the person submitting the report (eg. contact info, profession)
        - Administrative and sponsor information
- Reporting by Sponsors:
    - Sponsors are required to report SAEs that are unexpected to regulatory agencies within an adequate time period.
        - These reports are called Suspected Unexpected Serious Adverse REactions (SUSARs) in Canada and IND Safety Reports in the US.
    - Once the files have been submitted, the sponsor must notify all investigators participating in clinical trials of the investigational agent. Investigators should then notify their REBs or IRBs.
    - Reporting expectations:
        - Unexpected SAE that are not fatal/life-threatening: 15 calendar days for Health Canada/FDA, and 15 calendar days for sponsors
        - Unexpected SAE that are fatal/life-threatening: ASAP (but within 7 days, and a complete report within 8 days) for Health Canada/FDA, and 15 calendar days for sponsors
- Adverse Drug Reactions:
    - Once an AE has been linked to an agent, it is then considered an adverse drug reaction (ADR).
    - “In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established; all noxious and unintended responses to a medicinal product related to any dose should be considered adverse reactions.”
        - Response to a medicinal product: A causal relationship between a medicinal product and an adverse event is at least a reasonable possibility
    - WHO:
        - Adverse drug reaction: a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function
    - Side effect: used to describe negative, unfavorable effects, but can sometime refer to positive, favourable events
        - Generally not synonymous with adverse event or adverse

reaction
    - Reporting For Adverse Events for Marketed Products
        - Not all AEs are identified during clinical trials.
        - Health Canada and FDA require the continued reporting of AEs even after the product has been approved for marketing.
        - Methods:
            - CIOMS forms can be submitted via email
            - MedWatch monitors AE information
            - Form FDA 3500A can be completed
            - Voluntary reporting programs (MedEffect in Canada)
            - US Vaccine Adverse Event Reporting System (VAERS) is MedWatch equivalent for vaccines
            - CTEP also has a reporting system
            - NOTE: the FDA will accept SAE reports from international sites, if necessary
        - Sponsors must also submit periodic summary reports of AEs to the FDA, but are not required in Canada.
- Administrative Documents
    - The foundation of clinical research is in the documentation that is maintained throughout the research
    - The value of building a solid foundation right in the planning stages cannot be underestimated.
    - The development of administrative documents begins very early in planning stages during grant application and protocol development.
    - Clinical Trial Protocol:
        - The protocol is the document that is most referenced during a clinical trial.
        - Clinical Trial Protocol: a predefined plan of how the research will be carried out (kind of like a how-to manual)
        - Protocols are required to ensure that study-related activities are standardized so that results can be reproduced when the protocol is followed
        - Required sections by the GCP:
            - General information: study name, ID number, info about the sponsor, investigator, sites, etc.
            - Background information: past findings about the study product
            - Trial objectives and purpose
            - Trial design
            - Selection and withdrawal of participants: inclusion/exclusion criteria, when and how to withdraw participants, etc.
            - Treatment of participants: details about treatment administration, monitoring, etc.
            - Safety and Efficacy: methods for assessing efficacy and safety, especially for AEs
            - Statistics
            - Quality control/assurance
        - Frequently, protocols are drafted under a structured written plan for the study which helps with ensuring the protocol includes all important information
        - Protocol Deviations:
            - Deviations occur when the research veers form the approved protocol during the course of a study
            - Certain deviations may have significant impacts (data integrity, risk to participants, etc.)
            - The investigator should not implement any deviation from or

changes to the protocol without prior approval from the sponsor and REB.
        - Exception: if the deviation is to remove an immediate hazard to the participant
    - Deviations can occur any time during the conduct of a study.
        - Common example: meeting with a participant outside of the protocol-defined visit schedule
    - Risk of deviations can be mitigated by having a well-written REB approved protocol
- Investigator's Brochure (IB):
    - An IB is needed when a drug or IP is being developed for use in human participants
    - The purpose is to provide a summary of the information gathered during pre-clinical and clinical trial sand the information included should be relevant to the stage of development of the IP
    - The IB should be updated annually, and is a fluid document.
    - It is the responsibility of the sponsor to draft and provide the most up-to-date version of the IB to the investigator and the investigator is then responsible for providing the new IB to the local REB.
        - With sponsor-investigators, the IB should be procured from the commercial manufacturer
    - Development of IB is usually multidisciplinary, and requires input from:
        - Medically qualified personnel
        - Regulatory affairs
        - Research development teams
        - Clinical research staff
    - IB contents:
        - Note: all info needs to be simple to understand and concise
        - Title Page and Confidentiality Statement: includes sponsor name, product ID, version number, release date, edition number, etc.
        - Table of Contents:
        - Summary: Highlights the physical, chemical, pharmaceutical, pharmacological, toxicological, pharmacokinetic, metabolic, and other clinical information relevant to the IP
        - Introduction: includes chemical name, active ingredients, etc.
        - Physical, Chemical, and Pharmaceutical Properties and Formulation
        - Non-clinical study summary: dosage, route of administration
        - Effects on humans: summary of known effects to the product in humans as well as a summary of each clinical trial in which the IP has been used
        - Summary of Data and Guidance for the Investigator: up-to-date accurate summary of the clinical and non-clinical research data to date
    - While the IB is primarily for the investigators, REBs often review the IB in the process of deciding on ethics approval.
    - The IB is an important study document that should be carefully developed, but it is equally important to review and update the IB on a regular basis.
- Essential Documents:
    - Essential documents should tell a story showing how the trial was conducted, whether it was conducted in compliance with the protocol and regulations and should ensure a high level of data integrity in the information that was collected.
    - The general rule of thumb when conducting a trial is "document, document, document". <u>There is no detail too small and insignificant that should not be</u>

included in the documentation. The more details, the more thorough the documents.

- **In research, the only thing that remains to attest to its efforts are the documents!!!!!!**
- Responsibility:
    - Having a comprehensive master file is the responsibility of both the sponsor and the investigator.
    - Otherwise, both the sponsor and the investigator are required to keep a record of the location of their essential documents.
    - Documents must be searched easily, and need to be clearly identified and easily retrievable.
    - If a supplemental document, such as a Delegation of Authority Log, is necessary, the investigator is responsible for updating this.
        - Delegation logs should be created before study initiation, and it should be updated throughout the life of the study.
    - While sponsors are responsible for lots of the essential documents, they should not be controlled solely by them, and the investigator should have ongoing access to the documents, especially with regards to data.
        - If necessary, copies of documents may be used in place of the original.
        - Certified copy: “a copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describes the context, content, and structure, as the original.”
- Trial Master File Requirements:
    - Before the trial commences:
        - IB
        - Signed protocol
        - Information that is provided to study participants
        - Financial aspects, insurance statements, signed contracts, etc.
        - Ethics review, REB composition, etc.
        - Regulatory Authority Authorization (no objection letter by Health Canada)
        - Medical/Technical/Laboratory procedures, ranges, certifications
        - IP accountability documents
        - Randomization procedures
        - Pre-trial monitoring reports
        - Trial initiation monitoring reports
        - Relevant communications (for an audit trail)
    - During the trial:
        - IB updates
        - Revisions to any previously REB approved documents
        - Monitoring Visit Reports
        - Signed Informed Consent Forms
        - Source Documents
        - Signed, Dated Case Report forms (CRFs)
        - Safety Reporting (for AEs and SAEs)
        - Annual reports (progress of the study)
        - Subject tracking documents

                - Drug accountability
                - Signature sheets
                - Records of retained samples
            - After the trial:
                - Site accountability of investigational products
                - Completed subject ID log
                - Audit certificate (highlighting findings/issues during the audit process)
                - Final trial close-out monitoring report
            - Treatment allocation and decoding documentation
            - Final report by investigator for REBs and authorities
            - Clinical study report
    - Record retention:
        - The sponsor is responsible for ensuring that all trial related records are maintained appropriately throughout the duration of the study.
        - All trial related documents must be retained for a period of 15 years (Health Canada)
            - Sponsors may choose to “start the clock” for retention upon completion or termination of the trial instead of when the record is created.
        - Essential documents should keep their original format.
- Monitoring of Clinical Trials by Sponsors
    - Regulations require that sponsors monitor the investigations to ensure compliance with GCP and other standards.
    - Sponsor’s role
        - Canadian regulations require sponsors to conduct clinical trials in accordance with the GCP.
        - “Every sponsor shall ensure that a clinical trial is conducted in accordance with good clinical practices and, without limiting the generality of the foregoing, shall ensure that the clinical trial is scientifically sound and clearly described in a protocol; the clinical trial is conducted, and the drug is used, in accordance with the protocol and this Division; systems and procedures that assure the quality of every aspect of the clinical trial are implemented”
        - Purpose of trial monitoring:
            - To verify that:
                - The rights and well-being of human subjects are protected.
                - The reported trial data are accurate, complete, and verifiable from source documents.
                - The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).
        - US regulations require sponsors to monitor the conduct of the trials performed under an IND/IDE application
            - Clinical trial are monitored to ensure that
                - Participant’s rights and safety are being protected
                - The site is in compliance with FDA regulations and sponsor requirements
                - The investigator is meeting its obligations
        - No Canadian documents exist (regulations are in the GCP)
        - Assigning a monitor:
            - It is the responsibility of the sponsor to appoint a monitor for each study. Monitors should have appropriate training and scientific/clinical knowledge.

- Monitors should have a good understanding of:
    - The IP
    - Study documents
    - SOPs
    - GCP and other regulations
- Extent and types of monitoring:
    - Factors that affect monitoring:
        - Study objectives/purpose/design/complexity
        - Blinding
        - Sample size and trial endpoints
    - Types of monitoring:
        - On-site monitoring: performed at each site that is participating in the trial
            - This is generally the best option because the monitoring is more effective
        - Centralized monitoring: conducted remotely and allows for identification of missing data, inconsistencies, etc.
            - Reduces the need for in-person monitoring visits
    - Flexibility is allowed (there can be a mix of both types)
    - However, there needs to be a documented rationale for the type of monitoring in documents.
- Monitoring plans, templates, reports, etc.
    - A monitoring plan should include:
        - Brief description of the study
        - Purpose of the monitoring plan (eg. ensuring data quality)
        - Monitoring score and type of monitoring with a rationale
        - Frequency of monitoring
        - Site initiation information
        - Responsibility of all parties involved
        - Extent of source document verification
        - How areas of non-compliance will be addressed
        - Monitoring report requirements
        - Reference applicable policies and procedures
    - Monitoring plans are are fluid documents
    - Monitoring template: a document or checklist that identifies items that will be reviewed during each monitoring visit. It serves as a guideline for monitors to ensure that key documents and processes are assessed during the process
    - Monitoring reports: a detailed written report to be submitted to the sponsor and appropriate staff for trial oversight
- Sponsor Monitoring visits:
    - Site monitoring is important, but there are circumstances where the sponsor may determine that central monitoring instead of on-site monitoring.
    - Pre-study site visit:
        - At the outset of the clinical trial process, the sponsor chooses a pool of qualified individuals as potential investigators. The list is narrowed down, and the investigator is eventually determined.
        - Objectives:
            - Assess an investigator’s interest in conducting the study
            - Evaluate the facility and staff, determine whether they have the capacity to successfully conduct the trial
            - Determine whether they will be able to meet recruitment goals

        - Investigators and staff will be evaluated to see if they can perform the trial. This is based on:
            - Expertise
            - Availability of research participants
            - Adequate facilities
    - Site initiation visit:
        - After selecting an investigator and site, the sponsor proceeds with study initiation.
        - The primary objective of a site initiation visit is to train the investigator and study team to conduct the trial according to protocol requirements.
        - Training can include:
            - Detailed review of protocol
            - Instruction in completion of CRFs
            - Informing the site about drug accountability procedures
        - A review may be conducted as needed.
    - Routine monitoring visits:
        - The sponsor is also responsible for monitoring ongoing clinical trials.
        - Sponsor monitoring then would ensure that:
            - Health Canada/FDA requirements are being followed
            - Participant safety and welfare is being protected
            - The protocol is being strictly followed
            - Drug accountability requirements are followed
            - CRF data is being entered accurately
            - Patients have signed consent forms
            - Protocol violations are identified
            - Participant accrual rate is adequate
            - Participants are compliant
            - Changes in staff are documented and verify that replacement personnel are qualified
            - Facilities remain adequate
            - REB requirements are being met
            - SAEs are being captured, assessed, and reported promptly
    - Study close-out visit:
        - Objective is to ensure that the site has fulfilled all of its responsibilities
        - Visit typically includes:
            - Ensuring the appropriate disposition of all study supplies/IPs
            - Ensuring that all records are present and a storage location has been identified
            - CRFs are accurate and submitted to the sponsor
            - Signed consent forms for participants are reviewed
- Audits and Inspections in Clinical Trials
    - In the interest of human research participant protection and consumer safety, various regulatory agencies and research sponsors have a responsibility to verify the adequacy of study conduct.
        - This is conducted through inspections and **audits**.
    - Audits, inspections, and monitoring of clinical trials
        - Audit: a systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating

procedures (SOPs), GCP, and the applicable regulatory requirements.
    - Inspection: the act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CROs) facilities, or at other establishments deemed appropriate by the regulatory authority(ies)
    - Monitoring: the act of overseeing the progress of a clinical trial, and of ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.
- Sponsor Audits:
    - When a sponsor initiates an audit, it is for implementing quality assurance.
    - The sponsor should appoint independent auditors to ensure they are qualified by training and experience and must document these qualifications.
        - The extent of the audit should be based on the importance of the trial, complexity, number of participants, and regulation.
        - All findings must be noted in documentation and be reported to the investigator site and sponsor.
    - Issues of non-compliance that are identified should be promptly addressed to ensure compliance. In cases where non-compliance could potentially put participant safety at risk or jeopardize the integrity of the trial data, the sponsor must assess the issues to determine the root cause and implement corrective action.
    - Types of oversight:
        - Audits (sponsor or CRO): quality assurance that may change SOPs
        - Regulatory inspections (Health Canada): assure protection of research subjects, and may affect the agency’s decisions to accept the data
        - Monitoring (sponsor): refer to previous module
- Foreign inspections of canadian clinical sites
    - Inspections can occur when data from a Canadian clinical trial are being used to support a marketing application to a foreign regulatory agency. Inspections occur to ensure quality.
    - The inspections usually occur after the trials have been completed.
    - The FDA may issue warning letters to Canadian investigator sites, but enforcement actions are limited to restricting or refusing to accept future clinical trial data from a trial run by the investigator.
- Health Canada Clinical Trial Compliance Program
    - Health Canada has the authority to conduct regulatory inspections of clinical sites, and are carried out by the Regulatory Operations and Enforcement Branch (ROEB).
        - These inspections are typically conducted at investigator sites, and sponsors are encouraged to attend the inspections for learning.
    - Roughly 100 inspections are conducted per year. These sites are determined randomly, compared to the US.
    - Site selection is based on:
        - Number of clinical trials conducted at the site
        - Number of participants enrolled in the specific clinical trial
        - Number of SAEs
        - Observations made from past inspections
    - Additionally, compliance or investigative inspections may be conducted for addressing safety concerns.
    - NOTE: medical device trials are not considered for inspection by the CTC.

- Review of Regulatory Documents during Health Canada Inspections:
    - Inspectors will review all study records. Thus, it is important to ensure that all applicable essential documents are available for review, including supplemental documents.
- Inspection Exit Notice:
    - A verbal report on observations is usually presented to the investigator upon the completion of an inspection.
    - A final written inspection exit notice is also sent to the sponsor.
- Classification of Health Canada Inspection Observations:
    - Guidance document is titled: Classification of Observations Made in the Conduct of Inspections of Clinical Trials
    - Observation classifications:
        - Critical (risk 1): "An observation describing a situation that results in fatal, life threatening or unsafe conditions for subjects enrolled in a clinical trial. It presents an immediate or latent undue risk to the rights, health and safety of subjects. The conduct of unauthorized trials, adulteration, misrepresentation and falsification of records are also critical observations."
        - Major (risk 2): "An observation describing a marked deviation or deficiency, other than a critical one, that may result in undue health risks to the clinical trial subjects, in other persons or could invalidate the data."
        - Minor (risk 3): "An observation that is classified as not critical or major, but which indicates a deficiency and/or deviation from Division 5."
    - Ratings:
        - “C” (Compliant) at the time of the inspection, the regulated party has demonstrated that the activities it conducts are in compliance with the Food and Drugs Act and its associated regulations.
            - This doesn’t mean there are no observations or corrective actions required.
        - “NC” (noncompliant) at the time of the inspection, the regulated party has not demonstrated that the activities it conducts are in compliance with the Food and Drugs Act and its associated regulations.
        - Actions required from Health Canada “NC” Ratings:
            - Inspectors may recommend actions such as requiring the sponsor to undertake and implement immediate corrective action.
            - Inspectors may also recommend a Health Canada review of the study date.
            - Common NC issues:
                - Improper storage and/or documentation of IPs
                - Failure to re consent participants after protocol amendment
                - Insufficient study staff training
                - Lack of investigator oversight
                - Non-compliant to GCP
                - Infrequent/improper monitoring
                - Improper record retention practices
                - Discrepancies between source

documents and CRFs
- Lack of, or insufficient SOPs
- Deviations from protocol without waivers
- Protocol violations, not reported

- Health Canada inspection database
  - To be transparent, a clinical trial inspection database was launched by Health Canada in 2015.
  - The Drug and Health Product Inspections Database is an online tool that provides access to information related to clinical trials, medical devices, and drug manufacturing.

- US FDA Bioresearch monitoring program:
  - The bioresearch monitoring program, an FDA program, was established to routinely evaluate clinical investigators, investigative sites, IRBs, sponsors/CROs/monitors, and nonclinical laboratories.
    - Clinical investigator inspections usually take place after the New Drug Application (NDA) has been submitted for approval.
    - Other extensive inspections may be required if there is evidence of research misconduct.
  - Types of FDA inspections:
    - Study oriented inspections: directed toward review of study supporting pending marketing application such as NDAs, premarket approval applications (PMAs) or bioequivalence
      - Primary objective: verify data submitted to the FDA
        - However, other study-related practices are also frequently audited (eg. protection of research participants rights and welfare)
        - The FDA frequently inspect the top enrolling sites and randomly picks 10% of the remaining sites.
    - Investigator oriented inspections: directed at the specific clinical investigator conducting the trial:
      - Generally a result of complaints or known/suspected misconduct of investigators
  - Selection of Sites for Inspection:
    - Criteria considered:
      - Number of patients enrolled
      - Amount of “outlier” data
      - Numbers of participants responding to the study treatment
      - High numbers of dropouts
      - High numbers of adverse events
      - High numbers of protocol violations
      - Volume of work performed by the clinical investigator
      - Conducting research outside of the investigator’s speciality
      - Past inspection history
  - FDA Inspection process:
    - Generally, the FDA will notify the investigator about an impending inspection.
    - During the visit, the inspector will meet with the study coordinator and investigator. They will:
      - Evaluate the facility
      - Review regulatory records
      - Review participant records

        - Have discussion with key ancillary personnel
        - Evaluate IP accountability/control
        - Conduct an exit interview with the investigator
- Regulatory documents:
    - During FDA inspection, an in-depth review of regulatory documents helps the inspector recreate the events of the trial conduct.
    - Regulatory documents required:
        - IRB membership
        - IRB correspondence (submittal package, approval letter, progress reports, continuation reports, annual renewals, protocol amendments, IND safety reports, final reports, advertising)
        - IB
        - Investigator Curriculum Vitae (evidence of qualifications)
        - Protocol
        - Protocol amendments
        - Investigator Agreements (records that regulatory obligations are/were communicated and documented
        - Informed consent forms (blank)
        - Informed consent forms (filled out)
        - Correspondence (for creating a history of the clinical trial process)
        - IP records (paper trails)
        - Monitoring log
        - CRFs (Blank and completed)
        - Source documents
        - Laboratory certification
        - Laboratory normal value ranges
    - All these records are used to assist the FDA inspector in determining how activities and actions were performed during a clinical trial.
- Results and Consequences of FDA inspection findings:
    - If deficiencies in the research process are found, the inspector issues a written Form FDA 483, describing any inspectional observations that represent deviations from applicable statutes and regulations.
    - Following review, a letter may be sent to the investigator saying:
        - No Action Indicated (NAI): no violations
        - Voluntary Action Indicated (VAI): minor violations were noted and corrective action should occur, although is not required.
        - Official Action Indicated (OAI): significant violations were found during the inspection and the investigator must respond to the issues within a specific period (AKA warning letters)
    - Most serious violation consequences:
        - Initiation of investigator disqualification process
        - Warning letters
        - Rejection of study data
        - Deficiency letters
        - Withdrawal of marketing application
        - Application of Application Integrity Policy (AIP)
        - Civil penalties
        - Seizure of the product

        - Injunction
        - Prosecution
- OHRP Compliance Site visits:
    - The Office for Human Research Protections (OHRP) is an oversight agency that protects volunteers in “research that is conducted or supported by the US Department of Health and Human Services (DHHS)”. OHRP has jurisdiction over clinical trials conducted in the US with DHHS funding.
    - The office’s primary compliance department conducts inspections of IRBs.
    - OHRP compliance process:
        - The OHRP assurance process is designed to have institutions and IRBs register and agree that they will comply with requirements to protect human research subjects.
        - These institutional assurance documents often voluntarily extend OHRP oversight to all studies conducted by or at the institution, regardless of funding.
        - Much of OHRP oversight is conducted and resolved through correspondence with the institution.
        - OHRP conducts about 10 site visits per year.
    - An OHRP site visit can have severe effects on investigative sites.
        - Eg. it can result in marked changes in the institution’s IRB procedures and approval mechanism. The OHRP can suspend studies altogether, if necessary.
    - OHRP compliance outcomes:
        - Institution is compliant 🙂
        - Improvements are suggested (most common outcome)
        - Assurance restricted (some studies must stop until assurance is reinstated)
        - Assurance suspended (all studies must stop until assurance is reinstated)
        - Assurance withdrawn (all studies must stop until assurance is reapproved)
        - Temporary or permanent suspension of the investigator recommended, or DHHS peer-review groups notified about an institution’s or investigator’s past noncompliance before review of new projects
        - Debarment recommended (a government-wide sanction against an institution or investigator)
    - NOTE: if assurance is withdrawn or suspended, the institution can no longer qualify for DHHS grants for clinical research
- What do auditors/inspectors look for?
    - Ultimate objectives:
        - To assure adherence to regulatory requirements
        - To protect human research subjects
        - To assure data integrity and study validity