UVA
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Winter 2022

Inaugural Issue Remarks

Dear Readers,

When we first discussed the idea of a collaborative journal for healthcare professionals at the University of Virginia, we imagined an inclusive platform where students could not only share their research, but also their diverse opinions and experiences in healthcare. We believe that our students are immensely talented and deserve a medium to publish their work and share their unique voice. With this in mind, we encouraged students in medicine, nursing, and public health to contribute original primary research, review articles, and narratives pieces for our first issue.

We are eager to finally present to you the first inaugural issue of the University of Virginia Medical Student Review (UVAMSR). Our dedicated team of Associate Editors, Arts Directors, Managing Directors, and writers have worked tirelessly to produce a journal that we think you, the readers, will enjoy. We also would like to recognize and appreciate our faculty advisors who have made the launch of our journal possible. Inside you will find thought-provoking works that include the winning pieces from our recent narrative medicine and scientific research contests. We are honored to share these articles and hope you find them as engaging as we do.

We plan to continue expanding our journal and broaden the scope of the works that we share. We believe in sharing a variety of viewpoints and new ideas to inspire students from all backgrounds and circumstances to contribute to the field of medicine. We hope you enjoy the contributions of our students in this issue and feel encouraged to share your own works with us in the future. Thank you for reading!

Sincerely,

Sarah Swinehart　　Erica Mark

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RESEARCH

NARRATIVE MEDICINE

Difficulties and Ethical Dilemmas in Recruiting Residents to Participate in Research Studies

Elizabeth Driskill, MSDS, Seth Yarboro, MD, Keith Bachmann, MD
All authors are affiliated with the University of Virginia School of Medicine
1. Elizabeth Driskill, MSDS – third-year medical student
2. Seth Yarboro, MD – Associate Professor of Orthopedic Surgery
3. Keith Bachmann, MD – Assistant Professor of Orthopedic Surgery
Corresponding Author: Elizabeth Driskill, MSDS, ekd6bx@virginia.edu

ABSTRACT

The process of recruiting research participants can be difficult, especially when the population of interest has other characteristics that can limit their availability or create conflicts of interest. Our department conducted a study examining the association between performance on a series of manual dexterity tests and performance in the operating room among orthopedic surgical residents, but the study could not be completed due to an inadequate number of participants. Several factors contributed to this, including lack of financial incentives, inability of attending physicians to be involved in recruitment due to their role as evaluators, and the residents' busy schedules. Additionally, due to their status as trainees, residents are considered a vulnerable population, which presents further ethical dilemmas that need to be addressed throughout the research process. It must be ensured that residents do not feel coerced to participate due to inherent power dynamics within the medical field. Secondary effects of a resident's participation in the study such as loss of time for patient care and loss of confidence in their operative abilities must be mitigated. Potential solutions to improve recruitment could be to involve other residents in the recruitment process, offer incentives, and limit the time commitment of participation in the study. Research studies in medical education can offer valuable information about effective methods of teaching as well as useful metrics of evaluation, so it is important to address difficulties in participant recruitment so that further study can be completed in the future.

There are many obstacles that surface when recruiting research participants for clinical studies, and certain populations may be more difficult to recruit. Factors contributing to this difficulty include participant availability, general willingness to assist in clinical research, the conflict of educators as researchers, and lack of incentive. We proposed a study examining the correlation of performance on manual dexterity tests and surgical performance in the operating room, with the goal being to correlate performance on work medicine dexterity testing to performance in the operating room. This would allow for assessment of residents during the application process beyond their academic record and could provide useful information to students considering a career in a procedure-based field. The study involved recruiting orthopedic surgical residents to participate in a series of dexterity tests that took approximately one hour to complete. All orthopedic surgical residents would then be observed in the operating room by the principal investigator and have their performance scored.

Because the principal investigator is involved in resident education at the University of Virginia, he was recused from recruitment of participants to eliminate concerns that residents' participation status or performance could influence their resident evaluation. A medical student recruited participants by sending out emails to all orthopedic surgery residents (Figure 1). 3 out of 20 residents signed up and completed the dexterity tests. Due to the limited response and participation rate, the study could not be completed. There are several challenges and ethical dilemmas that arise when including residents as research participants, and these studies may require unique approaches to ensure adequate participation as well as protection of this potentially vulnerable population.

Recruitment processes for research studies are typically included in the research plan submitted to and reviewed by the Institutional Review Board.[1] The IRB bases their review on the Belmont Report drafted in 1979, which outlines the principles of respect for persons, beneficence, and justice.[2] These principles of research ethics also apply to the recruitment process, although their application to this facet of the research process is less clear. In terms of respect for persons, it is always important to approach participants with respect and without judgement during the recruitment process.[3] Participants should be recruited for studies that offer a benefit to them, whether for their overall health and well-being, education, or development of other useful skills. In this study, the benefit for participants would be to practice dexterity skills and potentially identify specific areas for personal improvement. The principle of justice is reflected in recruiting fairly and equitably among the eligible populations.

All researchers have difficulty recruiting participants, but junior investigators, such as graduate students, fellows, and faculty early in their career often face more recruitment challenges due to limited funding and fewer personnel resources.[4] In this study, a medical student sent out recruitment emails, which made it more challenging to recruit participants due to fewer social connections and less influence compared to more experienced researchers. Recruitment is often the most difficult part of a research study, as it frequently falls to more inexperienced researchers, and the process of recruitment is rarely outlined in the literature.[5] The more experienced researchers are more likely to have conflicts of education roles when it comes to recruiting trainees, creating a Catch 22 of participation. Financial incentives are accompanied by many ethical issues, especially as certain vulnerable populations may be more enticed to participate and thus can place themselves at higher risk (depending on the study) for the purpose of financial gain.[6] Financial incentives might have been a reasonable strategy in this study as there were limited risks involved in participation, but the process of receiving approval to provide financial incentives offers its own unique challenges. Additionally, surgical residents do not have ample free time, so they may not choose to spend it participating in research studies with limited incentive. Shamoo and Resnik outline a free wage model that guarantees research subjects a minimum wage equal to that of unskilled laborers to ensure that they receive their deserving share of the benefits of the research that they contribute to.[7] Conversely, offering financial incentives can present the issue of undue inducement. Undue inducement involves a person choosing to participate in a study where external factors may have an inappropriate influence on their decision-making process.[8] Financial inducement may not always be undue, but if a person is offered a large sum of money or is financially desperate, it could be considered undue in certain circumstances.[9] In this case, residents could be categorized as a financially desperate population, as many still have unpaid debts from medical school and undergraduate institutions and do not receive a substantial salary. There are also challenges that surface when seeking approval to provide financial incentives to participants, especially given media coverage of unethical behavior by physicians accepting profits for clinical trials.[10]

Another ethical concern when including residents as research participants is their status as trainees. Residents may feel unable to decline to participate due to fear that this would negatively affect their relationship with attending physicians or may feel pressured to participate if they perceive it could earn favor such as receiving higher grades, positive evaluations, or more research or clinical opportunities. In a study by Bonnano et. al, it was found that 76% of surgical residents believed that education research was important and that they should offer their participation.[11] However, 18% said they would feel coerced to participate and 21% said they would feel uncomfortable refusing to participate in a study conducted by a faculty member.[11] To avoid pressuring residents into participating in educational research studies, faculty members are often not involved in the recruitment process, which can lead to lower participation. In this study, residents received recruitment emails from a medical student that they did not personally know and thus were probably less likely to respond, especially given the number of emails they receive daily. This presents a unique dilemma in balancing faculty name recognition as a means of incentivizing residents to participate while also ensuring that residents do not feel compelled to participate as a result of a faculty member's higher status or other power dynamics at play.

One potential solution to improve recruitment would be to involve other residents in the research and recruitment process. This does not completely eliminate the issue of hierarchy, as residents who are earlier in their training may still feel pressured to participate to win the favor of their more experienced colleagues. However, peers or more senior residents do not have as much impact on performance evaluation as faculty. With either an attending physician or another resident involved in the research process, it is especially important to ensure that confidentiality is maintained. Most academic institutions require graduate students to receive training on research ethics,[12] but this is not always required to be repeated in frequent time intervals, and not all students take this training seriously. Due to their professional relationship with participants, it is likely that both attending physicians and residents would be excluded from administering the study and having access to participant data unless it was properly de-identified.

While most studies involving medical education do not present major risks to participants, it is important to consider secondary effects of a resident's participation in educational studies, such as loss of time spent caring for patients or for their personal leisure activities, embarrassment, and loss of confidence.[13] In this study, if a resident felt they did not perform well on the dexterity tests, they might begin to feel less confident in their abilities or less worthy compared to their peers. The goal of medical education research is never to cause residents to feel inadequate, unworthy, or uncertain of their abilities, and the parameters of each study must be carefully considered to ensure these negative effects are mitigated. This is especially important in the surgical field, as bullying and disruptive behavior have been shown to be prevalent in surgery in several studies; Gleason et. al found that 38% of general surgery residents reported experiencing public humiliation, most commonly perpetrated by attending physicians and upper-level residents.[14] A more optimistic side of the same coin could be a resident who is not satisfied with their current operative performance who performs well on a series of dexterity testing may gain confidence in their ability to work with their hands. It also provides an alternate task that involves no patient harm or "practice" on patients in a dry lab situation that would allow endless repetition for the resident to improve their skills. In order to make this a meaningful task for the trainee, a correlation to operative performance needs to be made to demonstrate that improvement in a simulation task correlates to operative improvement.

One strategy mentioned by Stovel et. al to improve participation was to provide novel educational experiences to participants that would not otherwise be offered during their medical education.[15] However, trainees might feel pressured to participate for fear of missing out on the opportunity if they do not participate. There are additional ethical considerations related to participation in a study that researchers believe will benefit trainees. For example, if practicing dexterity tests in this study correlated to certain measurable outcomes, like more favorable evaluations of residents' surgical competence, fewer physician-related errors during surgery, or faster completion of surgical cases (without compromising patient care), then it would be unethical to only offer this practice to select participants. This may require altering the study to include a cross-over design or to evaluate all participants before practicing the dexterity tests as well as afterwards, allowing anyone interested an opportunity to participate in the dexterity tests.

A study in South Africa evaluated different recruitment strategies to recruit nurses to participate in research involving filling out a questionnaire.[16] This population is similar to residents in terms of having limited free time, being financially vulnerable, and experiencing power dynamics within the workplace that could potentially influence their decision to participate in research. Strategies that they found helpful included involving nursing management in the recruitment and data collection process, using shorter questionnaires, and sending out reminders to participants.[16] Sending out reminders to participants did not prove to be extremely effective in our study, but it may have been helpful to involve attending physicians in the recruitment and data collection process, although this still presents ethical dilemmas that have been discussed above. It likely would have been useful to make the data collection process last for a shorter amount of time. Additionally, the study in South Africa mentions that face-to-face recruitment strategies proved to be effective, especially when involving a familiar person.[16] This could have been implemented in our study, but again could be viewed as unethical if residents felt obligated to participate when being recruited in person by someone with a higher status.

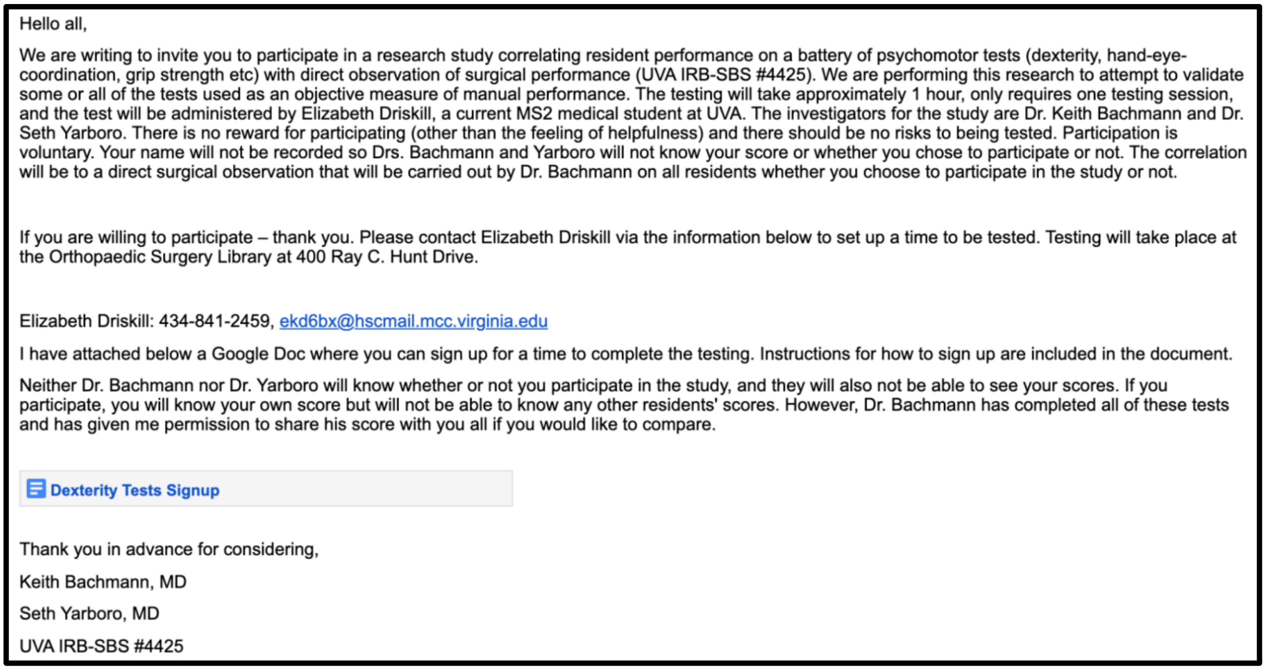
People can choose to participate in research for several reasons, and Singer and Bossarte highlight three important reasons: altruism, incentive, and interest in the topic being studied.[17] Participants must have sufficient information about the research study in order to weigh the benefits and risks of their participation.[18] However, information should be provided in a succinct manner to increase the chances that participants will be willing to read and comprehend it all. In the specific population of resident physicians, the most likely reasons for participation in research would be altruism and interest in the topic being studied, as there are rarely major incentives offered for their participation. There could be many reasons why residents choose not to participate in medical education studies, but several strategies exist to address residents' concerns about participating in studies, and these may be employed to achieve higher participation rates while also maintaining the ethical integrity of the study. It is helpful to disclose conflicts and privacy measures at the beginning of the study, gather only relevant data, and ensure that data is kept confidential (especially from any faculty members involved in resident education).[19] By considering these factors, research that overlaps with resident education can be carried out in a responsible, ethical, and effective way.

REFERENCES

1. Gyure ME, Quillin JM, Rodríguez VM, et al. Practical Considerations for Implementing Research Recruitment Etiquette. *IRB*. 2014;36(6):7-12.
2. Emanuel EJ, Grady C, Crouch RA, Lie RK, Miller FG, Wendler D. *The Oxford Textbook of Clinical Research Ethics*. OUP USA; 2008.
3. Brown BA, Long HL, Milliken N. What's to know about study recruitment? We asked recruiters. *Womens Health Issues Off Publ Jacobs Inst Womens Health*. 2002;12(3):116-121. doi:10.1016/s1049-3867(01)00145-1
4. Joseph RP, Keller C, Ainsworth BE. Recruiting Participants into Pilot Trials: Techniques for Researchers with Shoestring Budgets. *Californian J Health Promot*. 2016;14(2):81-89.
5. Patel MX, Doku V, Tennakoon L. Challenges in recruitment of research participants. *Adv Psychiatr Treat*. 2003;9(3):229-238. doi:10.1192/apt.9.3.229
6. Groth SW. Honorarium or Coercion: Use of Incentives for Participants in Clinical Research. *J N Y State Nurses Assoc*. 2010;41(1):11-22.
7. Shamoo AE, Resnik DB. Strategies to Minimize Risks and Exploitation in Phase One Trials on Healthy Subjects. *Am J Bioeth AJOB*. 2006;6(3):W1-13. doi:10.1080/15265160600686281
8. Grady C. Money for research participation: does in jeopardize informed consent? *Am J Bioeth AJOB*. 2001;1(2):40-44. doi:10.1162/152651601300169031
9. Macklin R. On paying money to research subjects: "due" and "undue" inducements. *IRB*. 1981;3(5):1-6.
10. Lemmens T, Miller PB. The Human Subjects Trade: Ethical and Legal Issues Surrounding Recruitment Incentives. *J Law Med Ethics*. 2003;31(3):398-418. doi:10.1111/j.1748-720X.2003.tb00103.x
11. Bonanno AM, Cook MR, Fair K, Dewey E, Kiraly L. Confidentiality concerns for surgical residents as educational research subjects: A pilot study. *Am J Surg*. 2020;220(3):630-633. doi:10.1016/j.amjsurg.2020.01.045
12. Swedan S, Khabour OF, Alzoubi KH, Aljabali AAA. Graduate students reported practices regarding the issue of informed consent and maintaining of data confidentiality in a developing country. *Heliyon*. 2020;6(9):e04940. doi:10.1016/j.heliyon.2020.e04940
13. Keune JD, Brunsvold ME, Hohmann E, Korndorffer JRJ, Weinstein DF, Smink DS. The Ethics of Conducting Graduate Medical Education Research on Residents. *Acad Med*. 2013;88(4):449-453. doi:10.1097/ACM.0b013e3182854bef
14. Gleason F, Malone E, Wood L, et al. The Job Demands-Resources Model as a Framework to Identify Factors Associated With Burnout in Surgical Residents. *J Surg Res*. 2020;247:121-127. doi:10.1016/j.jss.2019.10.034

15. Stovel RG, Ginsburg S, Stroud L, Cavalcanti RB, Devine LA. Incentives for recruiting trainee participants in medical education research. *Med Teach*. 2018;40(2):181-187. doi:10.1080/0142159X.2017.1395402
16. Khamisa N, Ilic D, Oldenburg B, Peltzer K. Evaluating research recruitment strategies to improve response rates amongst South African nurses : original research. *SA J Ind Psychol*. 2014;40(1):1-7. doi:10.4102/sajip.v40i1.1172
17. Singer E, Bossarte RM. Incentives for Survey Participation: When Are They “Coercive”? *Am J Prev Med*. 2006;31(5):411-418. doi:10.1016/j.amepre.2006.07.013
18. Khatamian Far P. Challenges of Recruitment and Retention of University Students as Research Participants: Lessons Learned from a Pilot Study. *J Aust Libr Inf Assoc*. 2018;67(3):278-292. doi:10.1080/24750158.2018.1500436
19. Boileau E, Patenaude J, St-Onge C. Twelve tips to avoid ethical pitfalls when recruiting students as subjects in medical education research. *Med Teach*. 2018;40(1):20-25. doi:10.1080/0142159X.2017.1357805

APPENDIX



Hello all,

We are writing to invite you to participate in a research study correlating resident performance on a battery of psychomotor tests (dexterity, hand-eye-coordination, grip strength etc) with direct observation of surgical performance (UVA IRB-SBS #4425). We are performing this research to attempt to validate some or all of the tests used as an objective measure of manual performance. The testing will take approximately 1 hour, only requires one testing session, and the test will be administered by Elizabeth Driskill, a current MS2 medical student at UVA. The investigators for the study are Dr. Keith Bachmann and Dr. Seth Yarboro. There is no reward for participating (other than the feeling of helpfulness) and there should be no risks to being tested. Participation is voluntary. Your name will not be recorded so Drs. Bachmann and Yarboro will not know your score or whether you chose to participate or not. The correlation will be to a direct surgical observation that will be carried out by Dr. Bachmann on all residents whether you choose to participate in the study or not.

If you are willing to participate – thank you. Please contact Elizabeth Driskill via the information below to set up a time to be tested. Testing will take place at the Orthopaedic Surgery Library at 400 Ray C. Hunt Drive.

Elizabeth Driskill: 434-841-2459, ekd6bx@hscmail.mcc.virginia.edu

I have attached below a Google Doc where you can sign up for a time to complete the testing. Instructions for how to sign up are included in the document.

Neither Dr. Bachmann nor Dr. Yarboro will know whether or not you participate in the study, and they will also not be able to see your scores. If you participate, you will know your own score but will not be able to know any other residents' scores. However, Dr. Bachmann has completed all of these tests and has given me permission to share his score with you all if you would like to compare.

Thank you in advance for considering,

Keith Bachmann, MD

Seth Yarboro, MD

UVA IRB-SBS #4425

Figure 1. Email template sent out to orthopedic surgical residents to recruit them to participate in the study.

The Many Faces of Urinary Extracellular Vesicles Artwork with description

Margaret Selesky[1], Luca Musante, PhD[2], Uta Erdbruegger, MD[3]

1. University of Virginia School of Medicine
2. University of Pennsylvania School of Veterinary Medicine
3. Division of Nephrology, University of Virginia Health

ABSTRACT

Extracellular vesicles (EVs) are small lipid bilayer-bound particles secreted from almost every type of mammalian cell. These vesicles exist in a nanometer-sized world, or 1,000,000 times smaller than 3/64th of an inch. Because of their size, transmission electron microscopy is one of the only ways to visualize these miniscule particles. Selected examples of cryogenic transmission electronic microscopy (cryo-TEM) photographs of urinary extracellular vesicles (uEVs) are presented here as "scientific artwork." Urinary EVs are a long-overlooked group which display remarkable visual diversity in size, shape, content density, and membrane structure. These vesicles have been studied in a variety of physiologic and pathologic states but little is known about what their visual diversity might imply.

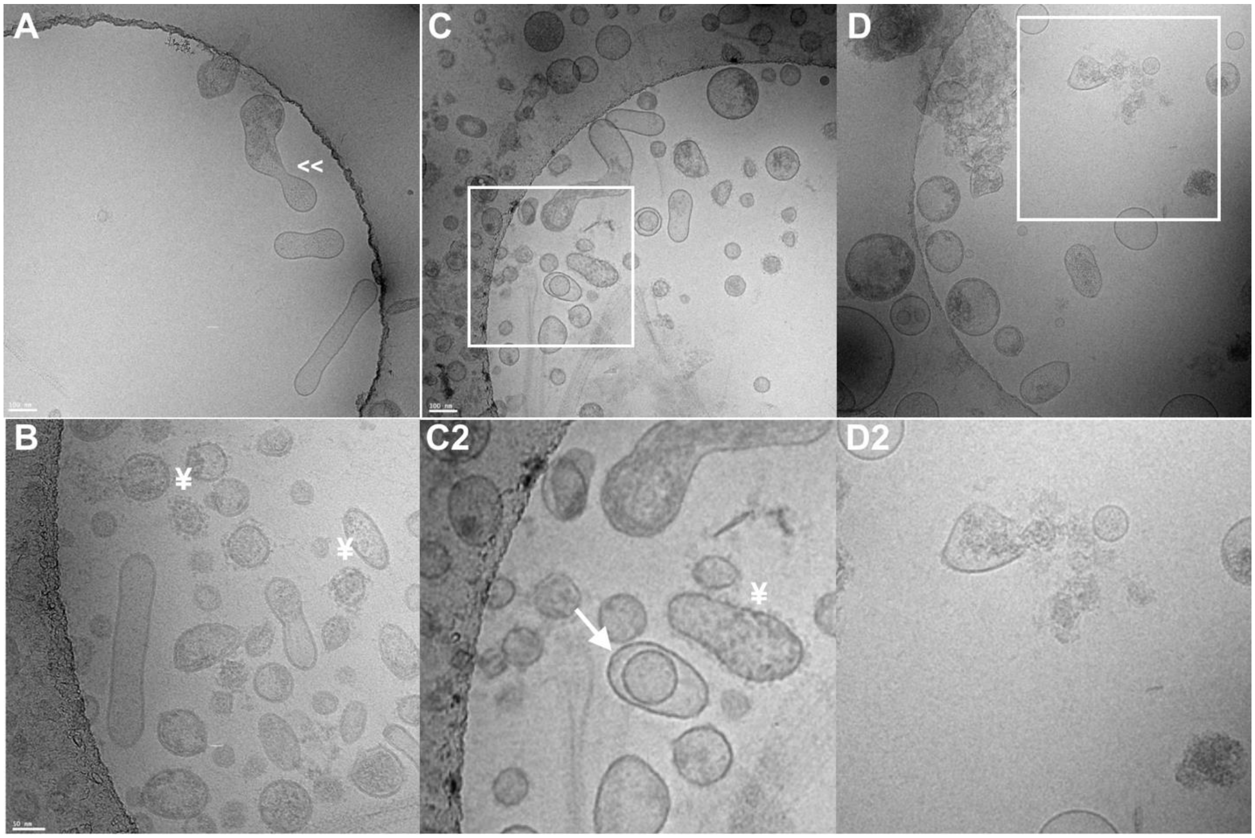
ARTWORK DESCRIPTION

Nature's artwork takes countless shapes and forms, even in unassuming places. Though urine is a waste product, the diversity of its contents and the data stored within them is staggering. Urinary extracellular vesicles (uEVs) are a heterogeneous group of particles which originate mostly from the cells of various structures within the urogenital tract, including the entire nephron from glomerular to collecting duct cells, the ureter, bladder, prostate, and urethra.[1] Extracellular vesicles are secreted from almost every type of mammalian cell.[2] Even in their creation, uEVs exhibit great diversity. There are three main families of extracellular vesicles: exosomes, microvesicles, and apoptotic bodies. Exosomes are formed during the maturation and release of multivesicular endosomes; microvesicles form via direct budding from the plasma membrane; and apoptotic bodies are released during the fragmentation of the cell membrane during apoptosis.[1,2] Initially seen as artifact or cell dust, uEVs have only recently been investigated as novel messengers. According to the International Society for Extracellular Vesicles' (ISEV) Rigor and Standardization Subcommittee, "in the last decade urinary extracellular vesicles were shown to mirror molecular processes as well as physiological and pathological conditions in kidney, urothelial and prostate tissue."[1] Mass spectrometry, Western blot analysis, and flow cytometry have already been used to characterize thousands of proteins in uEVs in a range of disease states, from diabetic kidney disease to prostate cancer to genetic causes of end-stage renal disease.[3-7] Not only do uEVs reflect disease processes in the urinary tract, they also behave as cell-to-cell communication mechanisms, shuttling information in the form of membranous and cytoplasmic proteins and other molecules like mRNAs and miRNAs.[8] In vitro studies have shown that uEVs can transport aquaporin 2, an important transmembrane water channel, between collecting duct cells, suggesting proximal collecting duct cells can influence the protein expression and thus the physiological functioning of distal collecting duct cells.[9]

Extracellular vesicles exist in a nanometer-sized world, or 1,000,000 times smaller than 3/64th of an inch. Because of their size, transmission electron microscopy is one of the only ways to visualize these miniscule structures. Selected examples of cryogenic transmission electronic microscopy (cryo-TEM) photographs of urinary EVs are presented here as "scientific artwork" which represents the beautiful diversity present in uEVs. The vesicles were obtained from a sample of urine from a healthy individual which was enriched using differential centrifugation at increasing rotational centrifugal forces, yielding a smaller and smaller pellet. This method has been successfully demonstrated to effectively enrich uEVs to allow for mass spectrometry and cryo-TEM of purified uEVs as described in (Musante et al, 2020).[10] These uEVs shown in our selection range in size from 60 to 250 nm in diameter and are delineated by an electrodense phospholipid bilayer membrane, generally round but sometimes with a more elongated or flattened shape (A-C), often with a smooth contour but occasionally with a rougher appearance and almost "spiky" membrane structures (¥). Urinary EVs can be electro-dense with varying density of granular matter and even house one or more smaller vesicles within (**arrow**). Smaller uEVs can be seen budding from larger ones (**<<**) and rupturing to spill their shapeless, coarse contents (D, D2). Cryo-TEM paints a striking visual representation of the range of uEVs which is evident in the data generated by other analytical methods.[4,6]

Clearly, urinary EVs are a rich source of information both for the human body's own cells and for researchers trying to extrapolate the process and progression of disease in the urinary tract, a feat commonly achieved through biopsy in the present day. Studies have shown uEVs have impressive diagnostic potential with clinical implications. In critically ill patients in the ICU, uEVs carry increased levels of an isoform of Na+/H+ membrane transporter in those with acute tubular necrosis (ATN) compared to those with prerenal azotemia, allowing for optimization of acute kidney injury (AKI) diagnosis.[11] Apical podocyte markers can be found in the uEVs of those with glomerular injury, and large scale proteomics have identified proteins which are elevated in uEVs of kidney transplant recipients undergoing acute T-cell mediated rejection.[12,13] These are just a few of many examples already discovered.[14] In contrast to invasive traditional tissue sampling, urine studies are easily performed as the substrate is in abundance, often discarded, and can be collected with no harm and minimal inconvenience to the patient. Urinary EVs, as site- and disease-specific markers, hold the potential to obviate the need for many kidney biopsies in the future, a change which would reduce complication rates like bleeding and may become the new "liquid biopsy."

Urinary EVs are a fascinating and exciting frontier in basic science research, and their profound beauty lies in the overwhelming diversity of form and function they exhibit. Little is currently known about what the difference in visual appearance might imply. In the same way we extrapolate the purpose of tissues from their form on a histology slide, will we one day be able to decode essential information about the health of a person's tissues from the appearance of their urinary extracellular vesicles?



REFERENCES

1. Erdbrügger U, Blijdorp C, Bijnsdorp I, et al. Urinary extracellular vesicles: A position paper by the Urine Task Force of the International Society for Extracellular Vesicles. *J Extracell Vesicles*. 2021;10(7):e12093. doi: 10.1002/jev2.12093.
2. Bruno S, Porta S, Bussolati B. Extracellular vesicles in renal tissue damage and regeneration. *Eur J Pharmacol*. 2016;5(790):83-91. doi: 10.1016/j.ejphar.2016.06.058.
3. Fujita K, Kume H, Matsuzaki K, et al. Proteomic analysis of urinary extracellular vesicles from high Gleason score prostate cancer. *Sci Rep*. 2017;7:42961. doi: 10.1038/srep42961.
4. Bijinsdorp I, Maxouri O, Kardar A, et al. Feasbility of urinary extracellular vesicle proteome profiling using a robust and simple, clinically applicable isolation method. *J Extracell Vesicles*. 2017;6(1):1313091. doi: 10.1080/20013078.2017.1313091.
5. Stokman M, Bijnsdorp I, Schelfhorst T, et al. Changes in the urinary extracellular vesicle proteome are associated with nephronophthisis-related ciliopathies. *J Proteomics*. 2019;10(192):37-36. doi: 10.1016/j.jprot.2018.07.008.
6. Guan S, Yu H, Yan G, et al. Size-dependent sub-proteome analysis of urinary exosomes. *Anal Bioanal Chem*. 2019;411:4141-4149. doi: 10.1007/s00216-019-01616-5.
7. Zhang J, Kumar S, Jayachandran M, et al. Excretion of urine extracellular vesicles bearing markers of activated immune cells and calcium/phosphorus physiology differ between calcium kidney stone formers and non-stone formers. *BMC Nephrol.* 2021;22(1):204. doi:10.1186/s12882-021-02417-8.
8. Ranghino A, Dimuccio V, Papadimitriou E, et al. Extracellular vesicles in the urine: markers and mediators of tissue damage and regeneration. *Clinical Kidney Journal*. 2015;8(1):23-30. doi: 10.1093/ckj/sfu136.
9. Street JM, Birkhoff W, Menzies RI, et al. Exosomal transmission of functional aquaporin 2 in kidney cortical collecting duct cells. *J Physiol*. 2011;589:6119-27. doi: 10.1113/jphysiol.2011.220277.
10. Musante L, Bontha S, La Salvia S, et al. Rigorous characterization of urinary extracellular vesicles (uEVs) in the low centrifugation pellet - a neglected source for uEVs. *Sci Rep*. 2020;10(1):3701. doi: 10.1038/s41598-020-60619-w.
11. du Cheyron D, Daubin C, Poggioli J, Ramakers M, Houillier P, Charbonneau P, Paillard M. Urinary measurement of Na+/H+ exchanger isoform 3 (NHE3) protein as new marker of tubule injury in critically ill patients with ARF. Am J Kidney Dis. 2003 Sep;42(3):497-506. 10.1016/s0272-6386(03)00744-3.
12. Hara M, Yanagihara T, Kihara I, et al. Apical cell membranes are shed into urine from injured podocytes: a novel phenomenon of podocyte injury. *J Am Soc Nephrol.* 2005 Feb;16(2):408-16. doi: 10.1681/ASN.2004070564.
13. Lim JH, Lee CH, Kim KY, et al. Novel urinary exosomal biomarkers of acute T cell-mediated rejection in kidney transplant recipients: A cross-sectional study. *PLoS One*.

2018 Sep 18;13(9):e0204204. doi: 10.1371/journal.pone.0204204.

14. Cricrì G, Bellucci L, Montini G, et al. Urinary Extracellular Vesicles: Uncovering the Basis of the Pathological Processes in Kidney-Related Diseases. *Int J Mol Sci*. 2021 Jun 17;22(12):6507. doi: 10.3390/ijms22126507

The Effect of Empagliflozin and Insulin on Vascular Biomarkers in Subjects with Type 2 Diabetes

Thi Nguyen[1], Kevin Aylor[2], Eugene Barrett[2]
University of Virginia [1]School of Medicine, [2]Department of Endocrinology and Metabolism
tpn2bs@virginia.edu, kwa2r@virginia.edu, ejb8x@virginia.edu

ABSTRACT

Objective: Sodium-glucose cotransporter 2 inhibitors (SGLT2is) for blood sugar reduction in type 2 diabetes (T2D) decreases incident cardiovascular events. At the microvascular level, diabetes is associated with increased levels of inflammatory biomarkers. We hypothesized that the SGLT2i, empagliflozin, would decrease inflammatory biomarker expression in T2D.

Methods: We screened T2D patient charts for study eligibility. Inclusion criteria included age 18-60 years, 6.5<A1C <9%, never on SGLT-2i, on stable dose of oral hypoglycemic agents and other medications >3 months, and BMI ≤ 45. Exclusion criteria included smoking in the past 6 months, taking insulin, BP >160/90, and history of severe medical issues. Before and following 12-week empagliflozin treatment, 10 participants underwent a 2-hour insulin infusion to measure metabolic and vascular insulin resistance. We held plasma glucose constant with variable glucose infusion. We used enzyme-linked immunosorbent assays (ELISAs) to determine the concentration of biomarkers before and after insulin infusion at baseline and after 12 weeks on empagliflozin.

Results: Empagliflozin lowered baseline and post-insulin ICAM-1 (p=0.00184) and increased VCAM-1 (p=0.000445). Insulin infusion consistently lowered PECAM-1 (p=0.00222,0.0275) and vasoconstrictor ET-1 (p=0.00794,0.00633) with or without empagliflozin treatment. E-selectin decreased and S100A8/9 increased during infusion both dates, although not significantly.

Conclusions: The ICAM-1 decrease indicates that empagliflozin decreases microvascular inflammation. Increasing VCAM-1 suggests oxidative stress is involved. The data suggests empagliflozin and insulin did not strongly impact S100A8/9 nor E-selectin. Overall, the biomarker response to empagliflozin was complex.

INTRODUCTION

Chronic conditions including diabetes affect a large proportion of the population[1]. Since 2019, over 37.3 million Americans have been diagnosed with diabetes[2]. Type 2 diabetes (T2D) accounts for 90-95% of these diagnoses[3]. Globally, the incidence of this condition has risen 102.9% from 1990 to 2017, with T2D accounting for most of the increase[4]. While type 1 diabetes (T1D) involves a lack of the regulatory hormone insulin, type 2 consists of the resistance of cells to insulin[5]. This inability to maintain a consistent blood sugar level over time can lead to symptoms including fatigue, excessive thirst and urination, and blurred vision[6]. Chronic complications include heart/kidney disease, nerve damage, and vision loss[7].

Although diabetes is often associated with symptoms and long-term complications, mechanisms at the capillary and endothelial levels are not as well delineated. After approximately ten to fifteen years of diabetes, pathologic changes occur in the microvasculature of multiple organs[8]. Little is known regarding biochemical changes that precede this process. At the microvascular level, endothelial cell adhesion molecules and other inflammatory biomarkers may shed light on this mechanism. These include Intercellular Adhesion Molecule-1 (ICAM-1), Vascular Cell Adhesion Protein-1 (VCAM-1), E-selectin, Platelet Endothelial Cell Adhesion Molecule-1 (PECAM-1), Endothelin-1 (ET-1), and myeloid-derived calcium-binding proteins, S100A8 and S100A9. These vascular biomarkers have many roles, including cell adhesion, vasoconstriction, leukocyte trafficking, and inflammatory processes[9]. These vascular biomarkers are also associated with cardiovascular events and other conditions[10].

In addition to lifestyle modifications, medications including insulin and metformin can help manage diabetes[11]. One newer class of drugs includes sodium-glucose cotransporter 2 inhibitors (SGLT2i), which help to regulate blood sugar by reducing glucose reabsorption in the proximal convoluted tubule of the kidney, thus increasing glucose and sodium excretion in urine[12]. Unexpectedly, SGLT2is have been associated with beneficial cardiovascular effects, including decreasing the incidence of congestive heart failure, myocardial infarctions, and mortality according to secondary prevention studies of cardiovascular disease in T2D[13]. This study aims to investigate the mechanism in which these effects occur– - specifically the impact of the SLGT2i, empagliflozin, on vascular stress biomarker expression in T2D. Compared to other SGLT2is, empagliflozin has particularly been demonstrated to improve cardiovascular disease[14]. We hypothesized that the SGLT2i, empagliflozin, would decrease circulating endothelial stress biomarker expression in T2D without known vascular disease.

METHODS

We investigated the effect of empagliflozin and insulin on inflammatory biomarkers with a prospective study. We conducted a chart review to screen for patients with T2D eligible for the study according to specific inclusion and exclusion criteria approved by the Institutional Review Board (IRB). Inclusion criteria included an age range of 18-60 years old, hemoglobin A1C (HbA1C) >6.5 and <9%, never on SGLT-2i (eg: Jardiance, Invokana, Farxiga, Steglatro), on stable dose of oral hypoglycemic agents and other medications >3 months, and a body mass index (BMI) of less than or equal to 45. Exclusion criteria included smoking presently or in the past 6 months, taking insulin, blood pressure >160/90, BMI of greater than 45, history of congestive heart failure, ischemic heart disease, severe pulmonary disease, liver or kidney disease. acute kidney injury, history of paraproteinemia syndromes such as multiple myeloma, hepatorenal syndrome or liver transplant, any vascular disease (such as myocardial infarction, stroke, peripheral vascular disease), history of cancer or psychiatric disease, presence of an intracardiac or intrapulmonary shunt, pregnant or breastfeeding, known hypersensitivity to perflutren (contained in Definity), screening O2 saturation <90%, and history of recurrent UTI/bladder/kidney infections (eGFR is below 45 mL/min/1.73). As of summer 2022, ten participants have joined the study. Study participants included 5 females and 5 males with an age of 53.89 ± 1.68 years and BMI of 33.7 ± 1.70 (Table 1). Upon admission, fasting blood glucose was 129.78 ± 13.37 mg/dL, systolic blood pressure was 128.78 ± 5.30, diastolic blood pressure was 74.11 ± 2.99, cholesterol was 150.11 ± 14.65 mg/dL, LDL was 85.78 ± 14.36 mg/dL, HDL was 37.44 ± 1.71 mg/dL, and triglycerides were 162.33 ± 26.41 mg/dL.

Participants underwent a 2-hour insulin infusion with a variable glucose infusion to keep plasma glucose constant to measure both metabolic and vascular insulin resistance both before and following 12 weeks with10 mg/day empagliflozin treatment. We collected blood samples at four time points at the 0 and 120-minute time points of the insulin clamp for both the baseline and 12 weeks on drug. We then performed enzyme-linked immunosorbent assays (ELISAs) to determine the levels of participants' serum inflammatory biomarkers: ICAM-1, VCAM-1, E-selectin, PECAM-1, ET-1, and S100A8 and S100A9 (Biotechne R&D Systems Quantikine Sandwich ELISA Kits). The concentration (ng/mL with the exception of ET-1 in pg/mL) of these biomarkers was measured at the 0 and 120-minute time points of the insulin clamp for both the baseline and 12 weeks on empagliflozin. A student's paired t-test (2-sided, Excel) was conducted on the data and statistical significance was considered to be p values less than 0.05. The power of the study was determined to be 80% with a p value of less than 0.05 and the number needed to complete the study was 14 based on an anticipated 40% change in microvascular blood volume.

RESULTS

Table 1: Baseline demographics of patients	
Sex	5 females and 5 males
Age	53.89 ± 1.68 years
Body Mass Index (BMI)	33.7 ± 1.70
Fasting Blood Glucose (FBS)	129.78 ± 13.37 mg/dL
Systolic Blood Pressure (SBP)	128.78 ± 5.30
Diastolic Blood Pressure (DBP)	74.11 ± 2.99
Cholesterol	150.11 ± 14.65 mg/dL
Low-Density Lipoprotein (LDL)	85.78 ± 14.36 mg/dL
High-Density Lipoprotein (HDL)	37.44 ± 1.71 mg/dL
Triglycerides	162.33 ± 26.41 mg/dL
A1C	6.84 ± 0.33 %

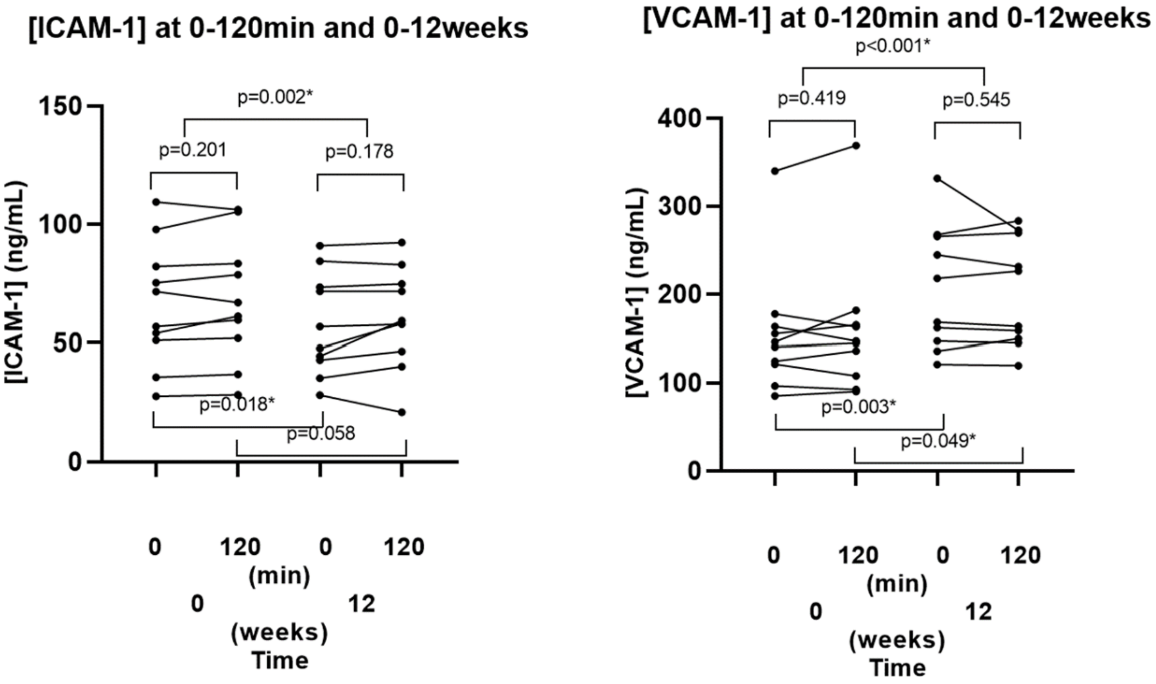


Figure 1: Empagliflozin treatment for 12 weeks decreased ICAM-1 and increased VCAM-1

The concentration of ICAM-1 at time 0 minutes of the insulin infusion decreased from 66.17 ± 8.69 ng/mL at baseline to 57.61 ± 7.14 ng/mL following 12 weeks of empagliflozin (p = 0.0184, Figure 1). The ICAM-1 concentrations at time 120 minutes of the insulin infusion were 67.85 ± 8.68 ng/mL at baseline and 60.45 ± 7.06 ng/mL. When both the time 0 and 120 minute concentrations for ICAM-1 were compared at baseline and 12 weeks, the p value was 0.00184. The concentration of VCAM-1 at time 0 minutes of the insulin infusion increased from 154.88 ± 23.65 ng/mL at baseline to 206.04 ± 23.24 ng/mL following 12 weeks of empagliflozin (p = 0.00322, Figure 1). The VCAM-1 concentration at time 120 minutes of the insulin infusion increased from 159.66 ± 26.59 ng/mL at baseline to 201.82 ± 20.40 ng/mL following 12 weeks of empagliflozin (p = 0.0486). When both the time 0 and 120 minute concentrations for VCAM-1 were compared at baseline and 12 weeks, the p value was 0.000445.

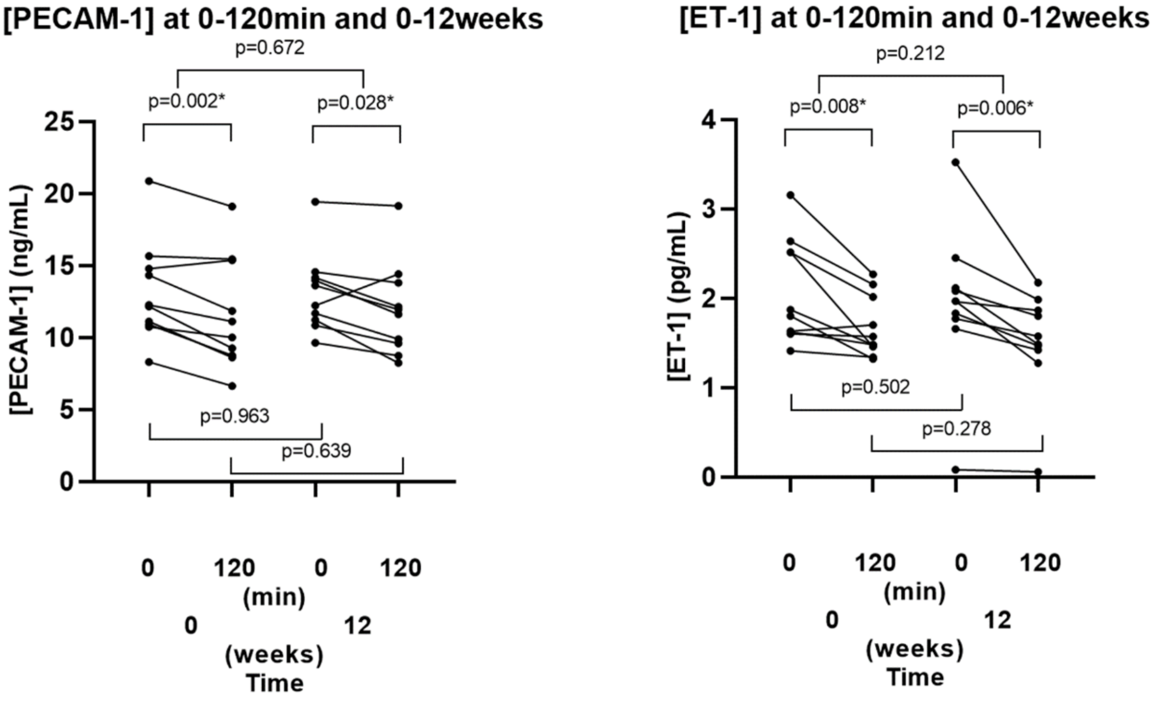


Figure 2: Insulin infusion decreased PECAM-1 and ET-1 before and after Empagliflozin for 12 weeks

At 0 weeks, the concentration of PECAM-1 at time 0 minutes of the insulin infusion decreased from 13.11 ± 1.17 ng/mL to 11.62 ± 1.29 ng/mL at time 120 minutes (p = 0.00222, Figure 2). At 12 weeks, The PECAM-1 concentration at time 0 minutes of the insulin infusion decreased from 13.13 ± 0.91 ng/mL to 11.95 ± 1.08 ng/mL at time 120 minutes (p = 0.0275). At 0 weeks, the concentration of ET-1 at time 0 minutes of the insulin infusion decreased from 2.08 ± 0.19 pg/mL to 1.68 ± 0.11 pg/mL at time 120 minutes (p = 0.00794, Figure 2). At 12 weeks, the ET-1 concentration at time 0 minutes of the insulin infusion decreased from 1.94 ± 0.28 pg/mL to 1.51 ± 0.19 pg/mL at time 120 minutes (p = 0.00633).

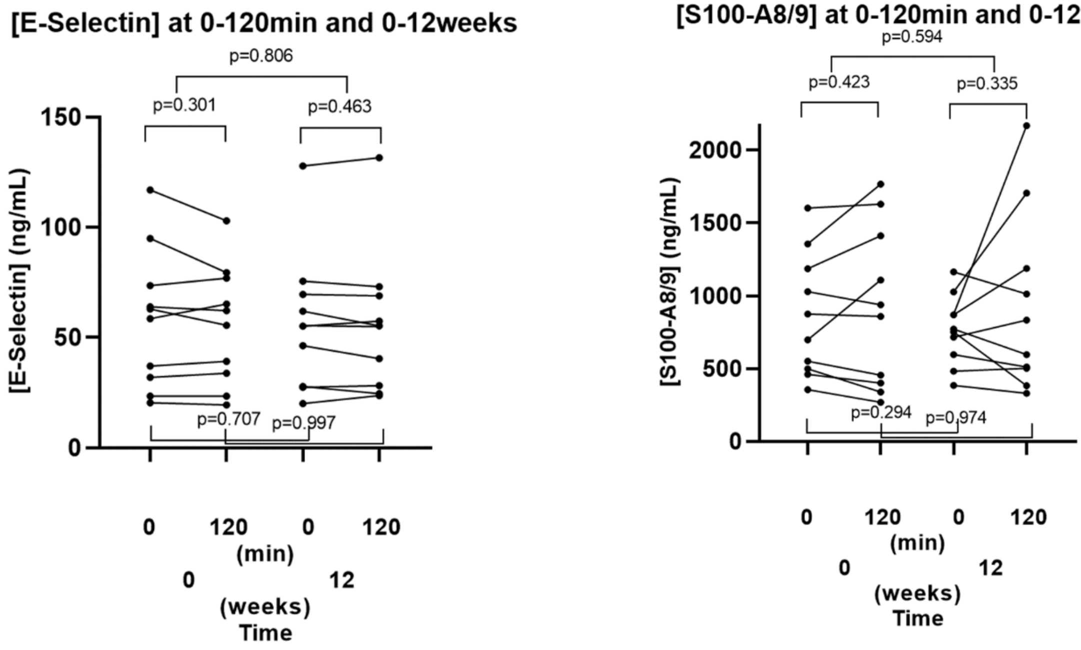


Figure 3: Circulating concentrations of E-selectin and S100A8/9 did not change significantly with either insulin infusion or Empagliflozin treatment

The concentration of E-selectin decreased from time 0 of the insulin infusion 58.37 ± 10.46 ng/mL to 55.80 ± 8.94 ng/mL at time 120 minutes at 0 weeks, although not statistically significantly (p = 0.301, Figure 3). At 12 weeks, the E-selection concentration at time 0 of the insulin infusion decreased from 56.71 ± 10.39 ng/mL to 55.82 ± 10.66 ng/mL at time 120 minutes, although not statistically significantly (p = 0.463). The concentration of S100-A8/9 at time 0 of the insulin infusion increased from 860.76 ± 140.41 ng/mL to 917.36 ± 184.08 ng/mL at time 120 minutes at 0 weeks, although not statistically significantly (p = 0.423). At 12 weeks, the E S100-A8/9 concentration at time 0 of the insulin infusion increased from 763.04 ± 79.05 ng/mL to 922.42 ± 203.16 ng/mL at time 120 minutes, although not statistically significantly (p = 0.335).

DISCUSSION

Although both ICAM-1 and VCAM-1 are cell adhesion molecules, ICAM-1 is expressed constitutively across more cell types and VCAM-1 is expressed after cytokine stimulation more specific to leukocyte adhesion[15]. ELISA assay results demonstrated that empagliflozin was associated with a statistically significant decrease in ICAM-1 (p=0.00184) and an increase in VCAM-1 (p<0.001) from baseline to 12 weeks on the drug. The decrease in ICAM-1 indicates that empagliflozin may decrease inflammation at the cellular level[16]. Based on current literature, an increase in VCAM-1 suggests that oxidative stress may be involved[17].

PECAM-1 is another cell adhesion molecule specific to endothelial cell junctions and involved in leukocyte trafficking, while ET-1 is a potent vasoconstrictor[18,19]. While there was no difference observed from baseline to 12 weeks, there was a statistically significant decrease in PECAM-1 (p=0.00222, 0.0275) and ET-1 (p=0.00794,0.00633) from 0 to 120 minutes for both dates. This suggests that while empagliflozin impacted ICAM-1 and VCAM-1, insulin had more of an effect on PECAM-1 and ET-1. This observation is consistent with what has been described physiologically, given that ET-1 causes vasoconstriction, and that insulin causes vasodilation[20].

E-selectin is expressed only on activated endothelium and its plasma concentration is positively correlated with glycated hemoglobin while S100A8/9 is a myeloid-derived calcium-binding protein specific to leukocytes and is involved in inflammatory processes[21,22]. E-selectin decreased and S100A8/9 increased during infusion both dates, although not significantly, suggesting empagliflozin and insulin did not impact S100A8/9 nor E-selectin.

According to the literature, hyperglycemia and T2D is associated with increased levels of pro-inflammatory markers. One study found increased ICAM-1, VCAM-1, PECAM-1, and E-selectin through flow cytometry when human umbilical vein endothelial cells were cultured in hyperglycemic conditions[23]. In a cross-sectional study of 30 T2D patients, serum ICAM-1, VCAM-1, and E-selectin determined with ELISAs were elevated[24]. Although there is limited data on how empagliflozin affects inflammatory biomarker expression using ELISAs in T2D patients with insulin infusion, this study is consistent with some previously reported findings. However, across research conducted in mice and humans, biomarkers before and after empagliflozin therapy have been mixed. In an observational and prospective study of 18 patients with T2D on 10 mg/day of empagliflozin, ICAM-1 levels measured by a flow analyzer decreased significantly but no effect was observed for VCAM-1[25]. In a diabetic mouse model, 6 weeks on empagliflozin at 20 mg/kg/day decreased VCAM-1, ET-1, and E-selectin expression quantified by quantitative Polymerase Chain Reaction (qPCR)[26]. A study on diabetic-induced mice treated with 10 mg/kg/day of empagliflozin for 20 weeks, demonstrated that empagliflozin reduced ICAM-1 and VCAM-1 measured by Western blotting[27].

Overall, despite the variety of results observed, there seems to be general agreement in the literature that serum levels of pro-inflammatory markers increase with T2D, and that empagliflozin is hypothesized to exert its beneficial cardiovascular effect by reducing the concentrations of such biomarkers.

In summary, although empagliflozin impacted the microvasculature environment in T2D without known vascular disease, the vascular biomarker expression was more complex than initially hypothesized. Empagliflozin lowered baseline and post-insulin ICAM-1 but raised circulating VCAM-1 and did not affect E-selectin or S100A8/9 concentrations. Insulin infusion consistently lowered PECAM-1 and ET-1 concentrations with or without empagliflozin treatment.

Although this study had quite a few statistically significant results, limitations of this work include a small sample size considering our current study had ten participants. Also, the biomarker response for each study participant could be correlated with vascular measures including blood pressure, artery stiffness, flow-mediated dilation, and pulse wave velocity, which were measured during the study. Preliminary data suggests that overall, empagloflozin is associated with increased microvascular blood volume (MBV), microvascular blood flow (MBF), and microvascular flow velocity (MFV) from baseline to 12 weeks. Considering diabetes is associated with a decreased microvascular volume, flow, and velocity, such observed changes further demonstrate the beneficial effects of empagliflozin[28]. Additional work could be done on other vascular, cell adhesion, and inflammatory biomarkers in an effort to obtain a more comprehensive picture of both microvascular and macrovascular effects. Furthermore, other drugs used for diabetes such as other SGLT2i or other classes of medications could be studied. While we had some interesting results, more research is necessary to further delineate mechanisms by which SGLT2is influence the microvasculature in T2D. Although this study is actively ongoing, this research contributes to the effect of an insulin clamp and empagliflozin on vascular biomarkers, which have not yet been previously described in the literature, and that initial results show that empagliflozin influences the microvasculature environment in T2D.

DISCLOSURES AND RELEASES

The authors report no conflicts of interest.

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REFERENCES

1. Raghupathi W, Raghupathi V. An Empirical Study of Chronic Diseases in the United States: A Visual Analytics Approach to Public Health. Int J Environ Res Public Health. 2018;15(3):431. doi:10.3390/ijerph15030431
2. American Diabetes Association. Economic Costs of Diabetes in the U.S. in 2017. Diabetes Care. 2018;41(5):917-928. doi:10.2337/dci18-0007
3. Westman EC. Type 2 Diabetes Mellitus: A Pathophysiologic Perspective. Frontiers in Nutrition. 2021;8. Accessed August 25, 2022. https://www.frontiersin.org/articles/10.3389/fnut.2021.707371

4. Lin X, Xu Y, Pan X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020;10:14790. doi:10.1038/s41598-020-71908-9
5. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna J Med. 2020;10(4):174-188. doi:10.4103/ajm.ajm_53_20
6. Ramachandran A. Know the signs and symptoms of diabetes. Indian J Med Res. 2014;140(5):579-581.
7. Jin Q, Ma RCW. Metabolomics in Diabetes and Diabetic Complications: Insights from Epidemiological Studies. Cells. 2021;10(11):2832. doi:10.3390/cells10112832
8. Diabetic Microvascular Disease: An Endocrine Society Scientific Statement | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic. Accessed July 28, 2022. https://academic.oup.com/jcem/article/102/12/4343/4604942
9. Theofilis P, Sagris M, Oikonomou E, et al. Inflammatory Mechanisms Contributing to Endothelial Dysfunction. Biomedicines. 2021;9(7):781.doi:10.3390/biomedicines9070781
10. Santos JC dos, Cruz MS, Bortolin RH, et al. Relationship between circulating VCAM-1, ICAM-1, E-selectin and MMP9 and the extent of coronary lesions. Clinics. 2018;73. doi:10.6061/clinics/2018/e203
11. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug-based therapeutics. Biomedicine & Pharmacotherapy. 2020;131:110708. doi:10.1016/j.biopha.2020.110708
12. Hsia DS, Grove O, Cefalu WT. An Update on SGLT2 Inhibitors for the Treatment of Diabetes Mellitus. Curr Opin Endocrinol Diabetes Obes. 2017;24(1):73-79. doi:10.1097/MED.0000000000000311
13. Padda IS, Mahtani AU, Parmar M. Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors. In: StatPearls. StatPearls Publishing; 2022. Accessed July 28, 2022. http://www.ncbi.nlm.nih.gov/books/NBK576405/
14. Rehman SU, Rahman F. Evidence-Based Clinical Review on Cardiovascular Benefits of SGLT2 (Sodium-Glucose Co-Transporter Type 2) Inhibitors in Type 2 Diabetes Mellitus. Cureus. 12(8):e9655. doi:10.7759/cureus.9655
15. Chiu JJ, Lee PL, Chen CN, et al. Shear Stress Increases ICAM-1 and Decreases VCAM-1 and E-selectin Expressions Induced by Tumor Necrosis Factor-α in Endothelial Cells. Arteriosclerosis, Thrombosis, and Vascular Biology. 2004;24(1):73-79. doi:10.1161/01.ATV.0000106321.63667.24
16. Canet F, Iannantuoni F, de Marañon AM, et al. Does Empagliflozin Modulate Leukocyte–Endothelium Interactions, Oxidative Stress, and Inflammation in Type 2 Diabetes? Antioxidants (Basel). 2021;10(8):1228. doi:10.3390/antiox10081228
17. Yuan T, Yang T, Chen H, et al. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. Redox Biol. 2018;20:247-260. doi:10.1016/j.redox.2018.09.025
18. PECAM-1 supports leukocyte diapedesis by tension-dependent dephosphorylation of VE-cadherin. The EMBO Journal. 2021;40(9):e106113. doi:10.15252/embj.2020106113
19. Chen YL, Rosa RH Jr, Kuo L, Hein TW. Hyperglycemia Augments Endothelin-1–Induced Constriction of Human Retinal Venules. Translational Vision Science & Technology. 2020;9(9):1. doi:10.1167/tvst.9.9.1
20. Manrique C, Lastra G, Sowers JR. New insights into insulin action and resistance in the vasculature. Ann N Y Acad Sci. 2014;1311(1):138-150. doi:10.1111/nyas.12395
21. Cominacini L, Fratta Pasini A, Garbin U, et al. Elevated levels of soluble E-selectin in patients with IDDM and NIDDM: relation to metabolic

control. Diabetologia. 1995;38(9):1122-1124. doi:10.1007/BF00402185

22. Frontiers | S100A8/A9 in Inflammation. Accessed July 28, 2022. https://www.frontiersin.org/articles/10.3389/fimmu.2018.01298/full

23. High glucose-induced endothelial microparticles increase adhesion molecule expression on endothelial cells - PMC. Accessed August 27, 2022. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6506489/

24. Hegazy GA, Awan Z, Hashem E, Al-Ama N, Abunaji AB. Levels of soluble cell adhesion molecules in type 2 diabetes mellitus patients with macrovascular complications. J Int Med Res. 2020;48(4):0300060519893858. doi:10.1177/0300060519893858

25. Canet F, Iannantuoni F, de Marañon AM, et al. Does Empagliflozin Modulate Leukocyte–Endothelium Interactions, Oxidative Stress, and Inflammation in Type 2 Diabetes? Antioxidants (Basel). 2021;10(8):1228. doi:10.3390/antiox10081228

26. Hogan MF, Hackney DJ, Aplin AC, et al. SGLT2-i improves markers of islet endothelial cell function in db/db diabetic mice. Journal of Endocrinology. 2021;248(2):95-106. doi:10.1530/JOE-20-0354

27. Zhou H, Wang S, Zhu P, Hu S, Chen Y, Ren J. Empagliflozin rescues diabetic myocardial microvascular injury via AMPK-mediated inhibition of mitochondrial fission. Redox Biology. 2018;15:335-346. doi:10.1016/j.redox.2017.12.019

28. Rendell M, Bergman T, O'Donnell G, Drobny E, Borgos J, Bonner RF. Microvascular blood flow, volume, and velocity measured by laser Doppler techniques in IDDM. Diabetes. 1989;38(7):819-824. doi:10.2337/diab.38.7.819

COVID-19 Vaccine Hesitancy and Source of Vaccine Information Among Communities in Virginia

Cameron Stadlin[1*], Caroline Cotton[1*], Mohan Nadkarni[2]
University of Virginia; School of Medicine[1], University of Virginia Health System[2]
*These authors contributed equally to this work.

ABSTRACT

Vaccination hesitancy has been recognized as a major barrier to achieving vaccination goals for COVID-19 across the United States. While there has been significant research on who is or is not receiving the vaccine, there is limited research concerning the source of COVID-19 information used by vaccine hesitant individuals and the reasoning these individuals are choosing to forgo vaccination. This study aimed to investigate these factors in Central Virginia surrounding Charlottesville, VA. Specifically, this study examined the relationship between vaccine hesitancy, the source of information for COVID-19, and the demographics of vaccine hesitant individuals in the greater Albemarle region as well as the reasoning for vaccination hesitancy. A total of 479 anonymous in-person and online surveys were conducted in Charlottesville and the surrounding counties. Participation was voluntary and surveys were conducted in Charlottesville and surrounding counties outside store fronts, at bus stops, and at University Medical Associates at the University of Virginia Health System. Lower vaccination rates were statistically significantly associated with Republican party affiliation ($p<0.05$) and lower educational attainment ($p<0.05$). Overall, using religious group as a source of information was associated with lower vaccination rates than doctor as source of information. Reasons for hesitancy included doubt that vaccination was necessary, concern over known and unknown side effects, concerns of the speed of the vaccine approval process, religious objections, and medical conditions.

Introduction

With the resurgence of vaccine-preventable illnesses around the world, the World Health Organization named vaccine hesitancy as a top ten threat to global health in 2019.[1,2,3] Although vaccine hesitancy is not a new phenomenon, public health concerns arose during the COVID-19 pandemic as vaccine hesitancy among adults in the United States became an urgent challenge that has yet to be completely resolved.[2] The difficulty with overcoming vaccine hesitancy, however, is the multiple factors that often influence those who are hesitant to receive vaccines. Issues with complacency (not perceiving a need for or value of the vaccine), confidence in the efficacy, safety, process of the vaccine, and convenience or access to receiving a vaccine, are all factors that can heavily influence the hesitancy to receive a vaccine.[4] In addition to these overarching barriers to receiving the vaccine, misinformation regarding vaccines and their benefits severely affects patients' understanding and overall buy-in.[5] Each of these factors have played a role in the hesitancy towards COVID-19 vaccination, and will most likely continue to influence acceptance of the ongoing and future deployment of COVID-19 vaccines, particularly relevant as Pfizer and Moderna request additional FDA booster approvals.

In the summer of 2021, only 52% of the adults in the United States population had been fully vaccinated for COVID-19, with similar rates in the state of Virginia as a whole.[6] The US vaccination rate has increased to approximately 63% of adults being fully vaccinated in the spring of 2022, but is still significantly below the vaccination goal of at least 80% of the population being fully vaccinated.[7] Previous studies on vaccine hesitancy in the COVID-19 pandemic have often focused on the demographics of the vaccine hesitant in the United States and around the world. These studies have shown an association between lower willingness to receive the COVID-19 vaccine and the following population demographics: black/African American individuals, unemployed individuals, women, Republicans, those with lower income than average, those who have received a high school education or less, rural populations, and non-healthcare workers.[8,9 10]

Other research has also shown that higher levels of knowledge concerning COVID-19 symptoms, the science behind its transmission, and the level the disease's contagiousness is correlated with increased protective behaviors such as social distancing and using hand sanitizers. This relationship highlights the importance of health literacy during this pandemic.[11] Additionally, having family members or friends affected by COVID-19 has been associated with higher rates of vaccination in comparison to those who do not know anyone affected by COVID-19.[12] However, rural Southern communities often do not have as much health literacy as other communities, and research of these communities has noted the negative impact of the politicization of the COVID-19 vaccines, the distrust of the government, and the indifferent view towards the COVID-19 pandemic on these rural communities' vaccine acceptance.[13] Gaining a deeper understanding of vaccine hesitancy in rural communities is critical to decrease the COVID-19 disease burden, as unvaccinated populations can serve as reservoirs of infection, thereby leading to increased variants and concerns for vaccine resistance, increased morbidity, and increased mortality.[12]

With this information, we recognized that data concerning an individual's specific reasoning for vaccine hesitancy and COVID-19 information sources of rural communities was lacking in scientific research. Thus, our research aimed to investigate who in Virginia was not getting vaccinated, why they are hesitant to receive the vaccine, and what the main sources of information were for these individuals when obtaining their COVID-19 information.

Methods

Study Design

This study surveyed a total of 479 individuals from June to August 2021. The inclusion criteria for the surveys were limited to participants above the age of 18 and residents of Virginia. Individuals who had received a COVID-19 vaccine and those who had not received a vaccine were surveyed. Verbal consent was obtained with every individual prior to initiating the in-person survey.

Data Collection

215 surveys were employed in-person through anonymous, self-completed questionnaires (unless participants were visually impaired in which surveys were completed verbally with aid of surveyors). The population of these participants included those living in Charlottesville, VA, and counties surrounding it including Albemarle, Greene, Louisa, Augusta, Nelson, Fluvanna, Orange, Madison, and Buckingham counties. Surveying was conducted in a variety of locations in these counties. Sites were asked individually if surveying at their location was acceptable. These site s included Charlottesville Area Transit bus stops, University Medical Associates at the University of Virginia Health System, IX Farmers Market of Charlottesville, Miller's Market of Louisa, Dillwyn Reid Market of Buckingham, Emergency Food Network of Charlottesville, Yoder's Market of Madison, Shoppers Value of Louisa.

264 surveys were employed online via Google Surveys. The population of these participants included those living in any county in the Commonwealth of Virginia. Google Surveys uses stratified sampling in combination with post-stratification weighting to ensure each survey's representativeness matches the target internet population.

Statistical Analysis

Vaccination rates between the subcategories of each demographic were compared with Fisher's Exact Test. Results were considered statistically significant with a p-value less than 0.05.

Results

For in-person surveys, information regarding age, race, county of residence, political affiliation, biologic sex, primary source of information regarding whether to receive the vaccine, and highest level of education completed was collected for everyone who completed the survey. Of the 215 individuals surveyed, 83.7% (180/215) were fully vaccinated (2 doses of Pfizer or Moderna or 1 dose Johnson & Johnson) and 0.5% (11/215) were only partially vaccinated.

The percent of each age group that had not received any vaccination was comparable across all surveyed ages, ranging between 6.3% and

18.6%, with the 18-24 age group having the highest vaccination rate and ages 25-39 and 75+ year olds having the lowest vaccination rate (Table 1). There was no statistically significant difference between the vaccination rates of the separate age groups.

For the racial distribution, the Black population had a higher population percentage without vaccination at 20%, followed by the white, non-Hispanic population at 16.3% (Table 2). Men also reported lower rates of vaccination as compared to females, with 19% having not received the vaccine vs. 14.5% respectively (Table 3). Again, there were no statistically significant differences between the not vaccinated rates of the categories in these groups.

Self-identifying Republicans reported the highest percentage of unvaccinated individuals at 27.3%, which was statistically significantly greater than unvaccinated Democrats at 9.2% (p = 0.0048). The rate of unvaccinated Republicans was significantly greater than the rates of those who identified with other political parties (Table 4).

Individuals whose highest level of completed education was middle school had significantly higher population rates without vaccination than those who had completed all other higher levels of education, including high school, associates degrees, bachelor's degrees, and post-graduate degrees (p = 0.04, p = 0.04, p = 0.05, p = 0.03). There were no statistically significant differences between any other subcategories (Table 5).

Buckingham, Greene and Nelson counties had the highest population rate without vaccination, 41.2%, 30.0%, and 28.6%, respectively. Orange and Madison had the lowest population rate without vaccination, 8.3% and 6.3%. (Table 6).

Many individuals used information from multiple sources when deciding whether to receive the vaccine, with the most common sources listed as family, TV/News, and doctors (Table 7). Those who received their primary source of information from their religious group had the highest population rate without vaccination (66.7%). Those who received information from their doctors or the internet had the lowest population rate without vaccination (11.9% and 11.8%).

Individuals who were surveyed in-person and were not vaccinated (16.35% of those surveyed) were asked why they did not receive the vaccine. 44.4% did not feel it was necessary, 37.0% were concerned about side effects, 25.9% had concerns about the vaccine approval process, 18.5% had religious objections, and 11.1% noted medical conditions (Figure 1). Similarly, of the 264 individuals who were surveyed online, 62.8% were fully vaccinated. Of the not vaccinated individuals, 38.1% were concerned about side effects, 34.2% had concerns about the vaccine approval process, 17.1% noted medical condition, 11.8% did not feel the vaccine was necessary (Figure 1).

Discussion

Vaccines are one of the most effective public health approaches to disease prevention, but their effectiveness is dependent on their use and is undermined by their refusal.[14] By August 2021, approximately 55% of Virginia residents were fully vaccinated and 62% had received at least one dose.[6] This was comparable to the United States as a whole, with 52% of the population having been fully vaccinated and 62% with at least one dose in August 2021.[15] Both of these total populations had significantly lower rates of vaccination than the in-person survey total at 83.7% fully vaccinated, but were relatively similar to the fully vaccinated rates of the online survey population. The discrepancy between the vaccinated totals of the in-person surveys versus the total population most likely reflects the higher level of comfortability with speaking about COVID-19 vaccination status among those who were already vaccinated. We specifically noticed that those who were already vaccinated were much more willing to partake in the survey as compared to those who were not vaccinated.

The other overall results of this study provide better understanding of vaccine hesitancy and although the nature of this study does not provide causal claims, the correlations in data provide further insight on predictors of vaccination and ways to best address hesitancy among certain communities. These results revealed three broader conclusions.

First, this study presents novel demographic trends in vaccine hesitancy that are specific to Virginians while reinforcing previous research on COVID-19 vaccination in the United States population. Of note, racial and ethnic minorities have been disproportionately affected by COVID-19, and the medical mistrust that has historically existed among these communities negatively affects their health behaviors such as vaccination, health, and quality of life.[16,17,18,19] Unfortunately, this trend continues to be evident throughout COVID-19, as multiple studies have shown the lowest rates of vaccination among Black Americans, as was shown in our study.[20,21] Nationwide surveys show similar vaccination trends with highest predictors of vaccine acceptance among Democrats and higher education achievement.[22,23,24] Interestingly, these same surveys showed that males were more likely to accept the COVID-19 vaccine in comparison to females. Our data showed a slightly higher vaccination rate among females, although this difference was not significant. Other predictors of vaccination that trend with those aforementioned include receiving the influenza vaccine in the years prior, having greater than 5 pre-existing medical conditions, and having a household income of $120,000 or more.[22,23,24] Correlations between low household income and lower vaccination rates are also reflected in these data in our study. The counties that were found to have the lowest reported vaccination rates all had median household incomes less than $50,000 and higher rates of poverty.[25] Other trends seen in these Virginia counties with lower vaccination rates include higher rates of medically uninsured and smaller percentages of the white, non-Hispanic population, those who have broadband internet subscriptions, and those who have a regular health care provider.[26] These demographic differences are highlighted in Table 8 comparing the counties of highest and lowest vaccination. The trends we saw in Virginia counties are comparable to lower vaccination rate trends in similar communities across the country.[27]

Addressing vaccination hesitancy in these populations is particularly important because of the disproportionate effect that COVID-19 can have on these areas with more barriers to adequate care and fewer resources. Notably, the mortality rates of COVID-19 in the United States in rural counties are significantly higher than metropolitan counties.[28] Alternative vaccine distribution sites such as mobile health units are an way to increase accessibility to rural residents and to areas of low income. These and other non-traditional testing and vaccination sites like barbershops, grocery stores, and salons have become popular in the United States and have significantly lowered barriers to access in many communities.[23,29] Many people we spoke to during our surveying took advantage of these sites and continuing to use these in future vaccination efforts would be beneficial for these populations. However, given that we still see significant hesitancy towards vaccination while access to vaccination sites has become remarkably easier, other factors of vaccine hesitancy must still be at play, as highlighted here in our research.

Secondly, these results provide a detailed understanding of how the source from which people gather their COVID-19 information is related to their vaccination status. T hose who received their information primarily from their religious group and leaders had the lowest percentage of vaccinated individuals. Many individuals turn to their religious community and leaders for solace and guidance in times of calamities, as exhibited throughout history from the Black Death in medieval Europe, to the 1918 flu in South Africa, to the September 11, 2001, attacks in the United States, and the COVID-19 pandemic is similar in this way.[30,31,32] Reports show that some religious leaders convince their congregation not to receive the vaccine, although this was the minority, while other leaders convey the vaccine as a message of hope.[33] However, no matter the message, religious beliefs and religious leaders' messages can play a considerable role in many peoples' decision making and are important factors to consider when trying to understand a patient's cultural background.[34] In fact, previous research on HPV vaccination has shown that rural residents wanted their pastors to discuss religious approval of the vaccine if they were uncertain about receiving this medical intervention.[35] A collaboration of science and religion in COVID-19 vaccine promotion could connect with many individuals in ways social media, the news, or even physicians cannot. With this, we reached out to over 20 churches for our surveys, however no location accepted our request to survey prior to the publication of this article. Physicians may look to connect with those in their own churches to provide education and could reach out to surrounding places of faith as well. Faith and religion are necessary for many in a time of crisis, in addition to the reliance on scientific information, and should not be overlooked when aiming to both understand and overcome vaccine hesitancy.

On the opposite end of the spectrum, those who used their doctors and the internet as their main source of COVID-19 information had the highest rates of vaccination. Although these are avenues for public health outreach that cannot change a vaccine-hesitant person's demographics, they can educate the less informed and challenge disinformation about future COVID-19 vaccines.[22] Educating patients during regular visits in the clinic or hospital should not be overlooked, as our surveyed showed that patients value and use their doctors' recommendations when making their own decisions. These conversations are vital to overcome health literacy barriers for many patients. Studies have shown that lower health literacy is associated with poorer health outcomes poorer, general health status, and even increased risk of death and hospitalizations.[36,37] In contrast, improved physician-patient communication has been associated with better outcomes, medication adherence, and self-efficacy in patients with hypertension, for example.[38] For the COVID-19 pandemic, low digital health literacy has been a direct contributor to the spread of COVID-19 information.[39] Having conversations about COVID-19 vaccination and related medical decisions with patients to address poor health literacy has potential to significantly benefit many individuals' overall health and health outcomes. The limitation with public outreach through physician visits and/or the internet is that many people in rural aspects of Virginia do not see a health provider on a regular basis, while others may not have easily accessible sources of internet. In these areas, healthcare providers must go directly to these populations to educate individuals about the vaccine, just as mobile vaccine clinics have gone to areas with greater barriers to care. Setting up information sites with physicians and/or medical students to create conversations with community members as we did during our surveying could promote these educating conversations where otherwise would not be possible.

Finally, our research presents specific reasons why those who were not vaccinated decided against receiving the COVID-19 vaccine. Religious objections, concerns about the vaccine approval process, questions of known and unknown side effects, medical conditions, and feelings that the vaccine is unnecessary were all reported reasons for declining to receive a vaccine, which is consistent with previous research.[40] We often heard comments comparing COVID-19 to influenza and feelings that media was exaggerating the danger of the virus. These views often coincided with feelings of government overreach and loss of personal freedoms. Side effect concerns were often two-fold: concerns of unknown long term side effects such as impacts on fertility, and concerns for short term side effects such as feeling ill following vaccination. On multiple occasions, we heard from those surveyed that he or she knew someone who "was killed by the vaccine," despite the CDC reporting a mere 13,273 preliminary death reports over more than 557 million vaccine doses - a rate of 0.0024%.[41] The exact causes of the deaths reported by some respondents cannot be further investigated from our standpoint. Regardless, it was apparent from our conversations with these individuals that death was perceived as a common complication of vaccination and this false perception has been a topic of anti-vaccination internet campaigns.[42]

One of the most common concerns expressed to us was unease towards the vaccine approval process with concerns that this was conducted in haste without adequate analysis of long-term side effects. Lack of understanding of the FDA vaccine approval process was evident in these discussions where community members often felt the vaccine was made too quickly, but they were unsure how long previous vaccinations they had received took to develop or how long of an approval process would make them feel more comfortable. The frequent discussion of vaccines throughout the COVID-19 pandemic has likely heightened people's awareness of the vaccine development process and raised concerns that have not previously been frequently discussed.[43] Additionally, political opinions were often heard by those expressing vaccine hesitancy, such as dislike and distrust of the current political administration and resentment of vaccine mandates. Religious objections were closely connected to using religious groups as a primary source of information. We heard on multiple occasions that individuals felt protected from COVID-19 due to their faith. Some participants wrote that he or she "received all protection they needed from Baptism", while others mentioned vaccination as circumventing "God's will and protection". Medical conditions, particularly autoimmune conditions, were occasionally noted as reasons for hesitancy, but this was a small minority of the hesitant population we encountered. Notably, the majority of the unvaccinated respondents described the concerns listed above as their reason for not receiving the vaccine in contrast to difficulties with finding vaccine sites, transportation, or financial concerns. This highlights the need for addressing the current causes of vaccine hesitancy, while maintaining access and outreach efforts.

This study does have limitations. The sample is limited to Virginia, and more specifically, to counties surrounding Charlottesville for the in-person surveys. The site locations were not completely random, as some sites we contacted would not allow surveying at their locations. Some of the specific populations in the study had very small sample sizes, notably the race subcategories apart from white, non-Hispanic and black, non-Hispanic as well as specific informational subcategories such as those who use their religious groups as their primary source of information. Response bias was another more obvious limitation. Many individuals did not want to speak with us about the vaccine and given that our percent vaccinated population is quite high compared to the total Virginia population vaccinated at the time (83% vs 62% respectively), we hypothesized that those who were already vaccinated and had supportive opinions about the vaccine were more willing to speak with us and complete our survey. This was one of the primary reasons why we conducted an online survey as well, to try and remove pressure associated with more difficult face-to-face conversations.

As the COVID-19 pandemic evolves and vaccines continue to develop, public health experts need to continue to create strategies for encouraging uptake of the vaccines. This study provides insight towards this goal, as well as highlighting the importance of physicians' roles in patient education concerning COVID-19 vaccination and other aspects of patients' health. The importance of physician-patient communication and working with patients' communities should not be overlooked, as understanding cultural backgrounds is an integral part to successful medical care. Finally, recognizing the rationale for opting against receiving a COVID-19 vaccine is necessary to guide future research and successful public health outreach.

Appendix

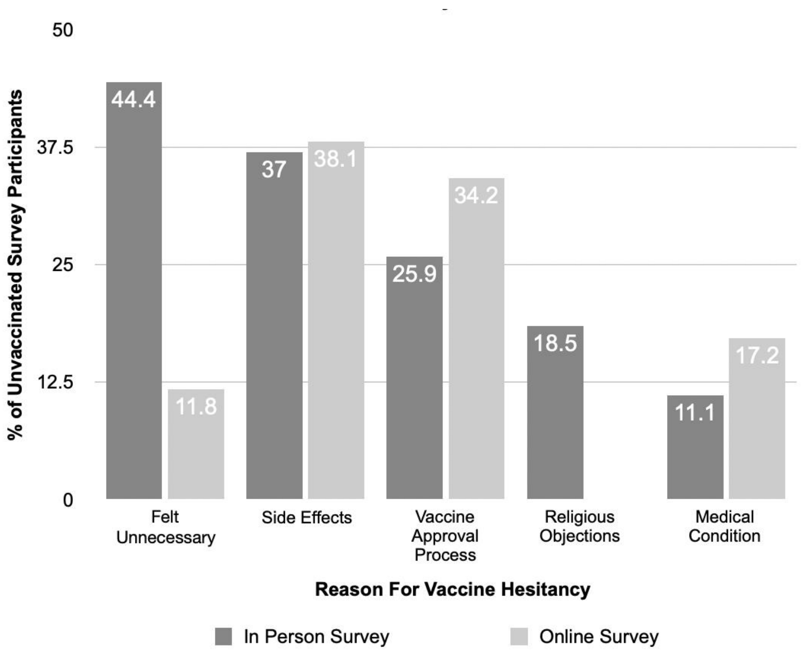

Figure 1: Reason for Vaccine Hesitancy. The reason for vaccine hesitancy in not vaccinated individuals of in-person and online surveys. Feeling that the vaccine is not necessary and concern for side effects were the most reported concerns for the in-person survey participants, while side effects and concerns about the vaccine approval process were the most listed concerns for the online survey participants.

Table 1: Age Differences in Vaccination Rates. The 18-24 age group had the lowest percent unvaccinated, however there were no statistically significant differences (p>0.05) in vaccination rates between age groups.

Age	**Number of People Surveyed**	**Percent of Subcategory, Unvaccinated (%)**
18-24	16	6.3
25-39	43	18.6
40-49	36	16.7
50-64	64	17.2
65-74	34	14.7
75+	22	18.2

Table 2: Racial/Ethnic Differences in Vaccination Rates. The Black, Non-Hispanic race/ethnicity group had the highest unvaccinated rate (20.0%), however there were no statistically significant differences ($p>0.05$) in vaccination rates between racial/ethnic groups.

Race/Ethnicity	**Number of People Surveyed**	**Percent of Subcategory, Unvaccinated (%)**
Black, Non-Hispanic	50	20.0
White, Non-Hispanic	153	16.3
Hispanic/Latino	2	0
Asian	9	0
Middle Eastern	1	0

Table 3: Sex Differences in Vaccination Rates. There were no statistically significant differences ($p>0.05$) in vaccination rate between biological sexes, despite males having slightly higher unvaccinated rates (19.0%) in comparison to females (14.5%).

Biologic Sex	**Number of People Surveyed**	**Percent of Subcategory, Unvaccinated (%)**
Male	84	19.0
Female	131	14.5

Table 4: Political Affiliation Differences in Vaccination Rates. Republican party affiliation is statistically significantly ($p<0.05$) associated with higher unvaccinated rates (27.3%) in comparison to Democratic party affiliation (9.2%).

Political Affiliation	**Number of People Surveyed**	**Percent of Subcategory, Unvaccinated (%)**
Republican	55	27.3*
Democrat	109	9.2
Independent	27	18.5
Non-voting	8	12.5
Prefer not to say	16	18.8

*: statistically significant, $p<0.05$

Table 5: Highest Level of Education Completed and Vaccination Rates. Middle school as the highest level of education achieved is statistically significantly ($p<0.05$) associated with higher unvaccinated rates (50.0%) in comparison to high school (25.4%), 2 year college (10.5%), 4 year college (16.7%), and Post-Graduate (14.3%) educational attainment.

Highest Education Level Completed	Number of People Surveyed	Percent of Subcategory, Unvaccinated (%)
Middle School	8	50.0*
High School	67	25.4
2 year College/Community College	19	10.5
4 year College	60	16.7
Post-Graduate	42	14.3

*: statistically significant, $p<0.05$

Table 6: County of Residence Differences in Vaccination Rates. Buckingham, Greene, and Nelson counties had the highest unvaccinated rates (41.2%, 30.0%, 28.6%), however there were not statistically significant differences ($p>0.05$) in county residency and vaccination rates.

County/City	Number of People Surveyed	Percent of Subcategory, Unvaccinated (%)
Buckingham	17	41.2
Greene	10	30.0
Nelson	7	28.6
Fluvanna	9	22.2
Augusta	9	20.0
Other	29	13.8
City of Charlottesville	94	12.8
Louisa	16	12.5
Orange	12	8.3
Madison	16	6.3

Table 7: Source of Information for Vaccine Decision and Vaccination Rates. Using a religious group as the primary source of vaccine decision information was associated with the highest unvaccinated rate (66.7%), but this difference was not statistically significant ($p>0.05$) compared to the other primary sources of information listed.

Source of Information	Number of People Surveyed	Percent of Subcategory, Unvaccinated (%)
Religious Group	9	66.7
Prefer not to say	3	33.3
Personal Opinion	11	27.3
Friends	34	26.5
Family	76	19.7
TV/News	52	19.2
Doctor	59	11.9
Internet	30	11.8

Table 8. Population Demographics of Buckingham, Madison, and Orange Counties. Buckingham, Madison, and Orange counties had the highest percent unvaccinated of counties surveyed. Demographics characteristics of these three counties are shown below.

Population Demographics of 3 Virginia Counties

	Buckingham	Madison	Orange
Living in poverty (%)	15.8	6.6	8.2
Bachelor’s degree of higher (%)	11.8	22.3	23.5
Broadband subscription at home (%)	63.9	70.7	78.3
White, Non-Hispanic (%)	63.2	86.9	82.1
Without health insurance and <65 years old (%)	13.4	12.9	11.7

References

1. World Health Organization. (2019). *Ten threats to global health in 2019*. Retrieved March 13, 2022, from https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019
2. Puri, N., Coomes, E. A., Haghbayan, H., & Gunaratne, K. (2020). Social media and vaccine hesitancy: new updates for the era of COVID-19 and globalized infectious diseases. *Human vaccines & immunotherapeutics*, *16*(11), 2586–2593. https://doi.org/10.1080/21645515.2020.1780846
3. Phadke, V.K.; Bednarczyk, R.A.; Salmon, D.A.; Omer, S.B. Association between Vaccine Refusal and Vaccine-Preventable Diseases in the United States:

A Review of Measles and Pertussis. *JAMA* 2016, *315*, 1149–1158

4. Troiano, G., & Nardi, A. (2021). Vaccine hesitancy in the era of COVID-19. *Public health*, *194*, 245–251. https://doi.org/10.1016/j.puhe.2021.02.025
5. User-Driven Comments on a Facebook Advertisement Recruiting Canadian Parents in a Study on Immunization: Content Analysis. *Tustin JL, Crowcroft NS, Gesink D, Johnson I, Keelan J, Lachapelle B JMIR Public Health Surveill. 2018 Sep 20; 4(3):e10090.*
6. Centers for Disease Control and Prevention. (2022, March 13). *Covid-19 Vaccinations in the United States, Jurisdiction*. Centers for Disease Control and Prevention. Retrieved March 13, 2022, from https://data.cdc.gov/Vaccinations/COVID-19-Vaccinations-in-the-United-States-Jurisdi/unsk-b7fc
7. (n.d.). COVID-19 Vaccine Tracker: See Your State's Progress." Mayo Clinic, Mayo Foundation for Medical Education and Research, https://www.mayoclinic.org/coronavirus-covid-19/vaccine-tracker. Retrieved March 20, 2022
8. Troiano, G., & Nardi, A. (2021). Vaccine hesitancy in the era of COVID-19. *Public health*, *194*, 245-251. Raja, A. S., Niforatos, J. D., Anaya, N., Graterol, J., & Rodriquez, R. M. (2021). Vaccine hesitancy and reasons for refusing the COVID-19 vaccination among the US public: A cross-sectional survey. *medRxiv*.
9. Cordina, M., Lauri, M. A., & Lauri, J. (2021). Attitudes towards COVID-19 vaccination, vaccine hesitancy and intention to take the vaccine. *Pharmacy practice*, *19*(1), 2317. https://doi.org/10.18549/PharmPract.2021.1.2317
10. Khubchandani, J., Sharma, S., Price, J. H., Wiblishauser, M. J., Sharma, M., & Webb, F. J. (2021). COVID-19 Vaccination Hesitancy in the United States: A Rapid National Assessment. *Journal of community health*, *46*(2), 270–277. https://doi.org/10.1007/s10900-020-00958-x
11. Kim, S., Capasso, A., Cook, S. H., Ali, S. H., Jones, A. M., Foreman, J., DiClemente, R. J., & Tozan, Y. (2021). Impact of COVID-19-related knowledge on protective behaviors: The moderating role of primary sources of information. *PloS one*, *16*(11), e0260643. https://doi.org/10.1371/journal.pone.0260643.
12. Khubchandani, J., Sharma, S., Price, J. H., Wiblishauser, M. J., & Webb, F. J. (2021). COVID-19 Morbidity and Mortality in Social Networks: Does It Influence Vaccine Hesitancy?. *International Journal of Environmental Research and Public Health*, *18*(18), 9448.
13. Alcendor D. J. (2021). Targeting COVID Vaccine Hesitancy in Rural Communities in Tennessee: Implications for Extending the COVID-19 Pandemic in the South. *Vaccines*, *9*(11), 1279. https://doi.org/10.3390/vaccines9111279
14. Piltch-Loeb, R., & DiClemente, R. (2020). The Vaccine Uptake Continuum: Applying Social Science Theory to Shift Vaccine Hesitancy. *Vaccines*, *8*(1), 76. https://doi.org/10.3390/vaccines8010076
15. Centers for Disease Control and Prevention. (n.d.). *CDC Covid-19 Data Tracker*. Centers for Disease Control and Prevention. Retrieved March 13, 2022, from https://tools.cdc.gov/api/embed/downloader/download.asp?m=415826&c=510934
16. Armstrong, K., Rose, A., Peters, N., Long, J. A., McMurphy, S., & Shea, J. A. (2006). Distrust of the health care system and self-reported health in the United States. *Journal of general internal medicine*, *21*(4), 292–297. https://doi.org/10.1111/j.1525-1497.2006.00396.x
17. Bogart, L. M., Ransome, Y., Allen, W., Higgins-Biddle, M., & Ojikutu, B. O. (2019). HIV-Related Medical Mistrust, HIV Testing, and HIV Risk in the National

Survey on HIV in the Black Community. *Behavioral medicine (Washington, D.C.)*, *45*(2), 134–142. https://doi.org/10.1080/08964289.2019.1585324

18. Jamison, A. M., Quinn, S. C., & Freimuth, V. S. (2019). "You don't trust a government vaccine": Narratives of institutional trust and influenza vaccination among African American and white adults. *Social science & medicine (1982)*, *221*, 87–94. https://doi.org/10.1016/j.socscimed.2018.12.020
19. Abedi, V., Olulana, O., Avula, V., Chaudhary, D., Khan, A., Shahjouei, S., ... & Zand, R. (2021). Racial, economic, and health inequality and COVID-19 infection in the United States. *Journal of racial and ethnic health disparities*, *8*(3), 732-742.
20. Bogart, L. M., Ojikutu, B. O., Tyagi, K., Klein, D. J., Mutchler, M. G., Dong, L., Lawrence, S. J., Thomas, D. R., & Kellman, S. (2021). COVID-19 Related Medical Mistrust, Health Impacts, and Potential Vaccine Hesitancy Among Black Americans Living With HIV. *Journal of acquired immune deficiency syndromes (1999)*, *86*(2), 200–207. https://doi.org/10.1097/QAI.0000000000002570
21. Nguyen, L. H., Joshi, A. D., Drew, D. A., Merino, J., Ma, W., Lo, C. H., Kwon, S., Wang, K., Graham, M. S., Polidori, L., Menni, C., Sudre, C. H., Anyane-Yeboa, A., Astley, C. M., Warner, E. T., Hu, C. Y., Selvachandran, S., Davies, R., Nash, D., Franks, P. W., … Chan, A. T. (2021). Racial and ethnic differences in COVID-19 vaccine hesitancy and uptake. *medRxiv : the preprint server for health sciences*, 2021.02.25.21252402. https://doi.org/10.1101/2021.02.25.21252402
22. Ruiz, J. B., & Bell, R. A. (2021). Predictors of intention to vaccinate against COVID-19: Results of a nationwide survey. *Vaccine*, *39*(7), 1080–1086. https://doi.org/10.1016/j.vaccine.2021.01.010
23. Fisher, K. A., Bloomstone, S. J., Walder, J., Crawford, S., Fouayzi, H., & Mazor, K. M. (2020). Attitudes Toward a Potential SARS-CoV-2 Vaccine : A Survey of U.S. Adults. *Annals of internal medicine*, *173*(12), 964–973. https://doi.org/10.7326/M20-3569
24. Meier, B. P., Dillard, A. J., & Lappas, C. M. (2021). Predictors of the intention to receive a SARS-CoV-2 vaccine. *Journal of public health (Oxford, England)*, fdab013. Advance online publication. https://doi.org/10.1093/pubmed/fdab013.
25. *Social Determinants of Health*. Virginia Department of Health. (2017, March 15). Retrieved March 13, 2022, from https://www.vdh.virginia.gov/data/social-determinants-of-health/
26. *Health Behavior*. Virginia Department of Health. (2021, May 20). Retrieved March 13, 2022, from https://www.vdh.virginia.gov/data/health-behavior/
27. Shekhar, R., Sheikh, A. B., Upadhyay, S., Singh, M., Kottewar, S., Mir, H., Barrett, E., & Pal, S. (2021). COVID-19 Vaccine Acceptance among Health Care Workers in the United States. *Vaccines*, *9*(2), 119. https://doi.org/10.3390/vaccines9020119.
28. Karim, S. A., & Chen, H. F. (2021). Deaths From COVID-19 in Rural, Micropolitan, and Metropolitan Areas: A County-Level Comparison. *The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association*, *37*(1), 124–132. https://doi.org/10.1111/jrh.12533.
29. COVID-19 mass vaccination involves unusual venues.*Traynor K Am J Health Syst Pharm. 2021 Jun 23; 78(13):1162-1164.*
30. Osheim, D.J. (2008). Religion and Epidemic Disease. *Historically Speaking 9*(7), 36-37. doi:10.1353/hsp.2008.0025.
31. Ai, A. L., Cascio, T., Santangelo, L. K., & Evans-Campbell, T. (2005). Hope, meaning, and growth following the September 11, 2001, terrorist attacks. *Journal of interpersonal violence*, *20*(5), 523–548. https://doi.org/10.1177/0886260504272896
32. Torabi, M. R., & Seo, D.-C. (2004). National Study of Behavioral and Life Changes Since September

11. *Health Education & Behavior*, *31*(2), 179–192. https://doi.org/10.1177/1090198103259183

33. Hegarty, S. (2021). 'The Gospel Truth?'Covid-19 Vaccines and the Danger of Religious Misinformation. *BBC News*.
34. Young, A., Ryan, J., Reddy, K., Palanee-Phillips, T., Chitukuta, M., Mwenda, W., ... & MTN-041/MAMMA Study Team. (2021). Religious leaders' role in pregnant and breastfeeding women's decision making and willingness to use biomedical HIV prevention strategies: a multi-country analysis. *Culture, health & sexuality*, 1-16.
35. Prusaczyk B. (2021). Strategies for Disseminating and Implementing COVID-19 Vaccines in Rural Areas. *Open forum infectious diseases*, *8*(6), ofab152. https://doi.org/10.1093/ofid/ofab152
36. Fabbri, M., Murad, M. H., Wennberg, A. M., Turcano, P., Erwin, P. J., Alahdab, F., Berti, A., Manemann, S. M., Yost, K. J., Finney Rutten, L. J., & Roger, V. L. (2020). Health Literacy and Outcomes Among Patients With Heart Failure: A Systematic Review and Meta-Analysis. *JACC. Heart failure*, *8*(6), 451–460. https://doi.org/10.1016/j.jchf.2019.11.007
37. Dewalt, D. A., Berkman, N. D., Sheridan, S., Lohr, K. N., & Pignone, M. P. (2004). Literacy and health outcomes: a systematic review of the literature. *Journal of general internal medicine*, *19*(12), 1228–1239. https://doi.org/10.1111/j.1525-1497.2004.40153.x
38. Tavakoly Sany, S. B., Behzhad, F., Ferns, G., & Peyman, N. (2020). Communication skills training for physicians improves health literacy and medical outcomes among patients with hypertension: a randomized controlled trial. *BMC health services research*, *20*(1), 60. https://doi.org/10.1186/s12913-020-4901-8
39. Bin Naeem, S., & Kamel Boulos, M. N. (2021). COVID-19 Misinformation Online and Health Literacy: A Brief Overview. *International journal of environmental research and public health*, *18*(15), 8091. https://doi.org/10.3390/ijerph18158091
40. Troiano, G., & Nardi, A. (2021). Vaccine hesitancy in the era of COVID-19. *Public health*, *194*, 245-251. Raja, A. S., Niforatos, J. D., Anaya, N., Graterol, J., & Rodriquez, R. M. (2021). Vaccine hesitancy and reasons for refusing the COVID-19 vaccination among the US public: A cross-sectional survey. *medRxiv*.
41. "Selected Adverse Events Reported after COVID-19 Vaccination." *Selected Adverse Events Reported after COVID-19 Vaccination*, Centers for Disease Control and Prevention, https://www.cdc.giv/coronavirus/2019-ncov/vaccines/safety/adverse-events.html
42. Prieto Curiel, R., & González Ramírez, H. (2021). Vaccination strategies against COVID-19 and the diffusion of anti-vaccination views. *Scientific Reports*, *11*(1), 1-13.
43. Swaney, S. E., & Burns, S. (2019). Exploring reasons for vaccine-hesitancy among higher-SES parents in Perth, Western Australia. *Health promotion journal of Australia*, *30*(2), 143-152.

The Impact of the Pandemic on My Life as a Nursing Student

By Rachel Rockecharlie

It was a Wednesday in my second year of college. Wednesday, March 11, 2020, to be exact. I was sitting in Starbucks with my roommate while we were on Spring Break and working on a project when we got the notification that UVA would extend its spring break and move classes online for the foreseeable future due to the Covid-19 pandemic. It was on this day that my life got turned completely upside down.

The following week, I had to move home from my apartment in Charlottesville and back into my childhood bedroom in Richmond. In addition to this move, I had to change my summer job plans. Though I had hoped to work as a patient care technician at a hospital, I quickly found out that many healthcare systems were on a hiring freeze, and there were not going to take on an untrained PCT amidst everything that was going on. As a result, I ended up working as a nanny for a family in Richmond.

As the end of summer rolled around and it was time to go back to school, I felt ready. Though I knew the semester would be anything but normal, I was excited to come back to Charlottesville and see my friends and engage in learning activities. My first semester back amidst the pandemic involved many Zoom classes, multiple saliva screenings, and a lot of food taken to go! Still, in spite of these changes, I feel fortunate to say that I was able to go back into the clinical setting. Though I had to be masked at all times, I loved being able to interact with real patients again, and to really remember why I wanted to go into nursing in the first place.

At the end of the semester, I packed my bags and went home. Because of the concern for spreading germs, the university asked everyone to stay home from Thanksgiving through Christmas and until after the new year. I felt sad that I would not be able to have a "Friends-giving" meal with my roommates or celebrate Christmas with my friends at a formal or other type of function. Nonetheless, I accepted what had to be. When January rolled around, I was offered the chance to receive the Covid-19 vaccine. I felt honored and blessed to have this opportunity, and despite some initial muscle aches and pain, the experience of receiving the shot was a positive one overall. Four weeks later, I received my second dose. Though that shot wreaked much more havoc on my body in the form of a fever, intestinal distress, a headache, and pain, it was all over within 36 hours, and for that, I am thankful. 36 hours of discomfort is much better than dealing with having Covid-19.

In considering all of these experiences, it is clear that a lot has happened in my life since the beginning of the pandemic, and events have unfolded in a myriad of socially-distanced ways.

I responded to the pandemic at first with sadness and loneliness, but later with hope. I know that as a result of this pandemic, my life will never again be the same. The pandemic has taken so much away from so many people, and for that I am frustrated and upset. However, in that negativity and in that darkness, I am working hard to find the light and a reason to have hope. With hope, I believe that good things can prosper, and it is my desire that things will get better and the world will turn a new leaf. Until then, I will work to focus on myself, prioritize schoolwork, and try to strengthen my relationships with my family and friends. The only way forward is through, so I know I have to keep pushing and keep hoping. There are better days to come.

All that said, I think I found myself playing the role of caretaker and counselor throughout the pandemic. My friends and family shared with me concerns and worries, and I also found myself beginning to take care of my younger siblings again, now that I was back at home.

I think that given the circumstances, I reacted in the way I did to this pandemic because, in a time where so much was unknown, I found comfort in falling back into old habits of caretaking, counseling, and listening to others. It was easier for me to focus on other people and their worries than to stop and think about how I was feeling or what I was worried about.

Though I felt anxious, worried, and upset at times, I also felt hopeful. I was hopeful that the healthcare workers would get the support they needed, that the vaccine efforts would roll out smoothly, and so much more.

I think resilient is a good word to use when I consider my responses and feelings and how they evolved as events evolved. At the beginning of the pandemic, there were so many unknowns. Now, however, we have adjusted to life in a pandemic, and I feel slightly less worried about the health and wellbeing of those around me.

In terms of experiences, I have had in the past that have shaped my understanding and response of today, I think the closest comparison I have to how I feel about the pandemic now was the confusion I felt during the 2009 swine flu pandemic. At that time, I did not know much about what was going on; I didn't understand why we were getting what I was told was a second flu shot or why we had to get the shot at the Richmond International Raceway with hundreds of other people instead of at the pediatrician's office. Fortunately, I have grown up since then, and I have more perspective on the situation and an understanding of pandemics and their implications in general.

In terms of if any experiences in nursing school have affected how I have viewed what has happened or how I have responded to what is happening, I would say that developing a better understanding of the social determinants of health and their impacts has really opened my eyes to inequities that exist and are only made worse by the pandemic. Similarly, I think learning about the importance of population health has really helped me to understand why we cannot just look at individuals and individual sickness. Rather, we must consider the whole community and get the whole picture. In other words, I know that when one person gets sick, it has a trickle-down effect and can impact many individuals. I also know that access to healthcare is another key component that is related to this pandemic.

In terms of my beliefs about the role of nursing in situations like this, I would say that nurses are absolutely critical. In the ICU and hospital settings, nurses have been the ones going in to check on patients who have Covid-19, and others are limited in going into patient rooms to preserve PPE. Clearly, the bedside care provided by nurses is critical. I think that nurses as leaders and educators also have an important role to play in this pandemic in the sense that they need to urge people to follow public health guidelines, and they can also work to dispel myths about the pandemic and the vaccine.

Though I already touched on some of the impacts of the pandemic on my life, I want to shed light more specifically on some of the more objectively positive and negative impacts. I loved being able to slow down and hang out with the children I nannied. I loved spending extra time with my family and having the opportunity to deepen my relationships with them. I loved eating take-out food in my pajamas on my couch instead of having to get ready to go out. Of course, I also felt lonely and isolated at times. I felt angry at my peers for not following public health guidelines. I felt frustrated that I could not have my normal college experience. Clearly, there are good and bad outcomes from this pandemic, but like I mentioned earlier, I have to focus on the good.

In terms of stresses I have had in responding to or helping others, I would say communication is a big concern. It is hard to communicate with people when you are so isolated and socially distant. However, I am doing the best I can with the energy and resources I have available.

In conclusion, I think my actions during this pandemic have matched my values. I have very much "walked the walk" in the sense that I have followed public health guidelines and have listened to science. Altogether, my experiences from this pandemic will affect me moving forward in that they will encourage me to never waste a single moment, to tell people how I feel, and to always work to consider the greater good whenever I think about my actions and how they might affect other people. I have learned so much from this experience, but perhaps most importantly, I have learned to prioritize my relationships and to not sweat the small things. I feel as though the only thing left for me to do is to continue to encourage people to follow public health guidelines and urge people to get vaccinated if they can and have not already.

I am excited to be a part of the change, and I look forward to doing what I can to stop this pandemic and help people become healthier.

55-word story

By Sebastian Dobrow

Stress. Personal stress, familial stress, stress about the planned, the unravelling, the known and the unknown.

Food in the fridge and the pantry. WiFi and online courses, central heat, no dependents. Am I even qualified to be stressed?

I think so. But also to be grateful. Things could always be worse, and they will be.

1045

By Alexandra DeFelice

ABSTRACT

As much as medical school tries, all the auscultation of your healthy classmates, all the OSCEs with your standardized patients, and all the hour-long lectures on grief, loss, death, and coping can only go so far, can only teach so much.

There are many skills in medicine that can only truly be learned through experience; this is, of course, one of the main goals of the clerkship phase of medical education. Clerkship is full of sometimes educational, sometimes remarkable, and often in-between "firsts": The student's first patient with this diagnosis, first day on that service; the first baby a student sees born—the first patient a student sees die.

For this author, the strangest, most notable, most memorable part of that first patient death was not the death itself nor the patient herself. Rather, it was walking into the next room and talking to the next patient. Patients die in the hospital every day, but there will always be more living patients than dead ones, and doctors—and students—tend to move toward the living.

This is a narrative account of moving from one room to another.

The family medicine intern was wearing bright orange-pink scrubs. The senior resident had complimented them just that morning— "Is that coral? Every day you have a different color! I need to start keeping track!"

And we had all laughed.

Now we were all walking away, and she was quiet, slow, tense. We all were, at least a little. The senior resident took a moment to walk beside me.

"Are you okay?"

"Yeah." It was immediate, instinctual. I didn't think before I said it. I wasn't thinking at all. It might have been a lie. I don't know. I wasn't sure I was okay—I wasn't even sure I was feeling.

But he accepted the answer and moved up to the attending. The attending had explained the exam to me as our coral-clad intern performed it.

"So, you check for a pulse. You listen to the chest. You look at the eyes, make sure they're fixed and dilated."

The family medicine intern had stood straight at that point, done with the exam.

"1045," she had said.

“1045,” the attending had repeated.

Now we were walking to the south tower. We passed the family in the hall. I saw the tears on their cheeks, but I couldn’t make it to their eyes. My gut twisted. I didn’t belong here. I wasn’t worthy of this.

And even now, thinking about myself. So selfish.

We were walking away, walking to the south tower. She had been in the north, way back when, at 1045. So we passed the elevators between, the visitor elevators. If we took them eight floors down, we’d be just outside the cafeteria—yes, of course, with just a few vertical seconds, we’d be released into a mass of relatively happy, relatively hungry people.

I’d never seen anyone crying in the cafeteria. Not that I’d noticed, at least.

But we didn’t go down the elevators—we only passed them. We passed the elevators. We passed the elevators, and I think it took an eternity. Yes. Yes, I remember. I remember it taking an eternity.

It was a miraculous eternity. Unbelievable. I’d say it was impossible, but it wasn’t, because it happened. We spent an eternity walking from north tower to south tower, and no one died. No one aged. No one even stopped to rest.

I’m not sure the rest of the team noticed it, how we spent an eternity walking past the elevators.

Our next patient was all the way at the end of the hall, as far into south tower as we could possibly go. I didn’t have a Spectra phone to call the nurse to meet us for rounds—the senior resident had taken it back. The senior resident had taken back his phone because he had been waiting for the call from the intern, who had kept her phone because she had been waiting for the call from the nurse, who had kept watch at the bedside that eternity ago back in north tower.

I think the other intern, the internal medicine intern, had a phone. But he was so far away, right there in front of me. He was so far away, those few feet away, and I didn’t remember how to walk faster. I didn’t remember how to talk. Could I even remember how to use a phone, if I somehow managed to obtain one?

I don’t know if anyone called the nurse. I don’t even know how we got to the room. I just know that we were in the room, suddenly, all staring at him. He had on the same dark red shirt and tan shorts as the day before when we had all stared at him in the corner of the gym-turned-emergency-department-overflow-area.

“We’re going to Narnia!” The interns had joked.

“Narnia?” The attending had asked. “That’s what they’re calling it?”

And then we had walked through the ER and by the escalators and through the lobby and into a hallway and through some doors and the pattern of the floor and the color of the walls kept changing and then I had looked up and it wasn’t the ER at all, but there were patients and machines and little portable medical privacy barriers separating them from one another and nurses walking to-and-fro amidst the strange arrangement.

Narnia.

But now he wasn't in Narnia anymore—no, he was in the real world. He had made it from Narnia to the MRI, from the MRI to the elevators, and from the elevators to the south tower.

And he kept his clothes, somehow, for some reason. It's better for me that he kept his clothes, since it gave me something else to try to focus on while the attending talked.

For he had made it all the way from Narnia, and it wasn't even good news. He was the third one this week. The words still mattered to me—they had to. The words have to matter. The words must always matter. I must never let the words cease to matter.

The words of the attending were light, familiar, insignificant: Jaundice, mass, hospice.

But the words from the patient were heavy, new, memorable: The oncologists had been by, he felt fine, this was so sudden.

He wasn't upset, but the words mattered.

The words mattered because they were his. And the attending might say the exact same thing to each patient, but no two patients say the exact same thing back.

The attending was so normal. He wasn't calloused, not that I could tell. But he was solid, strong, resistant. The words couldn't weigh him down. The woman from the north tower—and her family—they couldn't reach him. They couldn't bother him. He was impervious.

But they bothered me, and they bothered the coral intern.

I heard the senior resident ask her a little while later if she was okay, just like he had asked me. She told him she was. But then he left—and I think another eternity might have passed, I'm not sure—and I heard her talking to the other intern, just the three of us in the room.

"Yes, I had patients die when I was a student. But have you ever had to tell the family? I had to tell the family."

And she kept saying it.

"I had to tell the family. Have you ever had to tell a family that? I had to look at them and tell them."

The internal medicine intern hadn't had to tell the family yet. He didn't know.

And I didn't know. I hadn't even seen a family yet, not before that day. But now I have seen a family, and I won't forget. I remember that family—her family. And I remember her.

I remember him, too, the man in the dark red shirt. The man in the dark red shirt from Narnia.

I remember hearing him talk to the attending. I remember trying to focus on his clothes but failing—I remember thinking about the prognosis as they talked. I remember talking about it the day before, when we were discussing one of our other pancreatic cancer patients.

"10 in 100 are eligible for a Whipple," the attending had said. "And of those 10, only 3 have good outcomes."

He had paused to let me process, and then he had said what had already flashed through my mind— “It’s a 3% chance.”

As we stood there, I stared at the man from Narnia and thought about the woman—do I still call her a woman? —over in north tower, the one whose family I could barely look at.

She didn’t have pancreatic cancer, but they really weren’t that different. They were the same, with enough time. They were 97% the same.

His wife had been with him in Narnia, but she wasn’t in the room now. Maybe it was the eternity we took walking over. Maybe the eternity accelerated his cancer and scared her away—it’s understandable to be scared.

I wasn’t scared, though. I wasn’t anxious or on-edge. I wasn’t even spooked. The family in north tower—and the maybe-woman—weren’t scaring me away. I didn’t feel frightened. I didn’t feel overwhelmed.

I just felt inadequate.

What have I done to be worthy of telling people their poor prognosis, warning them of their impending death? What have I done to deserve the honor and humility of standing next to a dying person, of watching someone die, of so intimately knowing the time of death?

What have I done, to be there at 1045?

And since I’m here—as ridiculous as that is—what am I supposed to do? When these things happen, what am I supposed to do?

Do I forget about the woman in north tower as soon as her family is behind me? Do I keep her until I knock on the door of the man from Narnia? Do I bring her with me into the room?

I don’t think it’s that last one.

I don’t *think*, but I don’t know.

For if I leave her outside in the hall, or if I drop her off completely way back at the feet of her crying family, then what is the point? And if I shake her off that quickly, that effortlessly—if I fight so hard to get rid of her easily—then will the words of the man from Narnia still matter?

I must never let the words cease to matter.

Every person in medicine goes through it. Everyone knows. Everyone has been there. I’m sure of it. So why had no one told me? Why had no one taught me?

I had been taught how to feel the pulse and auscultate the chest and inspect the eyes. I had been taught how to get from north tower to south tower, which elevators went where, how the rooms were numbered. I had been taught to gel in and gel out. I had been taught to knock, to give my name, to explain my role. I had even been taught how to strip a person down to nothing more than an age, sex, and chief concern. And I had been warned—I had been warned of the lack of sleep, of the unique stress, of the endless critique, of the gravity and the seriousness, of the special trust, of the empathy and how easily it is lost.

But no one had taught me how to walk out of one room and into another. No one had warned me how complicated it can be.

Not necessarily difficult, just complicated.

No one had told me about the stillness, about the eternity, about the patients' complete lack of knowledge of one another. The man from Narnia didn't know about the crying family on the other side of the tower—he didn't know that we had just watched someone die.

And even now I'm not sure: I'm not sure what to do with the woman from north tower. I am sure that I still want to call her a woman; I am sure that I don't want to forget her.

But I'm not sure where she belongs—I'm not sure if she's allowed to come into the next room with me. I'm not sure if she's allowed to stand there with me and make sure the words still matter, and I'm not sure if the words will still matter if she doesn't.

The senior resident could tell that no one had told me about these things—he could tell that I didn't know—and that's why he had asked. The internal medicine resident could tell, too, and he asked me as well, once we finished rounding and were heading back to the workroom.

"You okay?" It was a very soft, very casual, very calm, very kind, and very sincere two words, but I could still only muster one in response.

"Yeah."

Compassion, Lemonheads, and 15 Articles Published Last Year

By Sarah Marion

"Cranes in my culture symbolize hope and healing, so I thought I would give this to you." My mentor reached over the bed and handed her patient a purple paper crane no bigger than the size of her petite palm. The patient held it tenderly with a wide smile and moistening eyes, while Dr. C continued. "While my family is Japanese, I'm also from the Midwest so I'm a hugger. So if it's alright with you, would you mind if I came over and gave you a *big* hug?" The patient nodded appreciatively and Dr. C, who probably was a foot taller, leaned over and wrapped her arms around the oversized gray hospital gown that draped the patient's shoulders.

I watched their embrace while standing awkwardly in the corner. Suddenly, I found myself crying, presumably because of the tangible compassion of their tender moment. I quickly dried my eyes with the back of my hand, took a deep breath, and followed Dr. C out of the exam room as the visit finished.

Dr. C whispered to me as we speed-walked back to the office, "That woman has been through a lot. Her cancer has come back several times and she's one of the few who don't tolerate the radiation very well. But her treatment is done today so she gets to ring the Radiation Oncology Bell– not to be confused with the Cancer Bell in hospital hallways." She clarified, "the RadOnc Bell is for anyone who finishes their treatment. You don't have to be 'cured' or 'have won the battle,' or whatever. I mean, you know how I feel about the concept of cancer battles." I nodded smugly, feeling special that I knew Dr. C well enough to know her opinions on cancer metaphors, and even better to know which ones she didn't like. I understood that war metaphors fail those who "lose the battle" to cancer. Cancer takes many people's lives, there should be no "loser" identity attached to those who die. Frankly, it's plain old luck that determines cancer survival. Maybe luck plays a role in actual wars, too, but that's another conversation.

My day with Dr. C went by fast, which was a saving grace as they went from 7 am to 9:45 pm. I powered through, fueled by: an everything bagel that Dr. C bought the clinic that morning, a coffee cake that one of her patient's left in the breakroom, snickers bars that Dr. C had on her desk, two boiled eggs that I bought at the café upstairs, and several cups of pecan caramel coffee. One would have thought I was carbo-loading for a crew meet the next day, but I suppose any healthcare provider could appreciate that it was just an overbooked clinic day. You know, only 31 patients.

By around 4pm, I had learned the script for patient visits: ask about how they're doing, ask if they have any questions, answer those questions, re-inform them about their treatment plan (or if they're finishing up, discuss scheduling for a follow-up), and finish with a brief physical exam. Visits were quick yet somehow unrushed. Dr. C was able to be fully present with each patient. She gave them the space and opportunity to voice any concerns, ask what was on their mind, and feel indubitably and meaningfully heard. Dr. C's workflow was extremely impressive.

As I shadowed Dr. C for those 15 hours, I hoped her patience, compassion, work ethic, knowledge, and humor would spill over into my future practice. I find her incredibly inspiring. She lost her husband to cancer, which sparked a drastic career change from graphic artist to radiation oncologist. Her creative background is still evident in her funky eyeglass choices and bowl of lemonhead candies that matches her yellow-accented office.

Her career as a physician is intriguing beyond her motivation to become one. She published 15 articles last year, which means she published 15 articles during a global pandemic. Meanwhile, many of us – apologies for speaking for you – were making circumstantial COVID-19 excuses about why our discipline was lackluster. She runs professional Twitter accounts, takes on summer interns, presents at board meetings, walks across Manhattan before work, advocates for affordable health care, guest stars on podcasts, donates to charities, maintains veganism, and amid all of this, taught me how to hustle.

I would argue Dr. C's hustle is absolutely ideal but also impossible to replicate. I see her hustle as the model to strive for, knowing anything close would still be considered an achievement (the whole "shoot for the moon, land amongst the stars" mantra). Perhaps more impressive Dr. C's work ethic is the unabating and pervasive compassion and personhood she exudes with each of her patients. Compounding this demeanor with her incredible CV makes her all the more admirable. Imagine getting peer review feedback saying, "nice try, but here are 8 more comments to respond to," before walking into the exam room of your anxious new patient who has 9 questions to respond to. That's 17 answers needed and it's not even 8am. Imagine also having your summer intern follow you around this whole time. The intern is trying her best, really, trust me, but she too has 10 points needing clarity. 8 plus 9 plus 10. These numbers even underestimate the work of a physician, especially one who is conducting research and taking on interns— and anyone who can do it with grace is deserving of a Nobel Peace Prize.

Shadowing Dr. C gave me more than just exposure to the niche field of radiation oncology. It enabled me to see how compassion and quirks can be worn on the sleeves of a doctor's white coat. It taught me how character can be leveraged to provide high quality, personalized cancer care. Dr. C's patients appreciated her funky glasses, paper cranes, midwestern hugs, jokes about "COVID weight," and empathetic ear. They showed their gratitude through pizza purchases for staff lunch and homemade coffee cake for the breakroom. Multiple people literally tapped me on the shoulder in exam rooms to let me know how delighted they were to have Dr. C as their doctor.

I, *too*, was delighted to have Dr. C as my mentor. I got to observe her in the exam room, but I also got to listen to her argument against cancer metaphors as we walked down the hallway, and watch her perform clinical target volume contouring for radiation dosing in her office. Shadowing Dr. C, for even just that one day at the Memorial Sloan Kettering Cancer Clinic, convinced me that my true self – empathy, quirks, worth ethic, and all – will be welcomed graciously by my future patients.

Community and COVID: The Musings of a First-Year Medical Student in the Era of COVID-19

By Mackenzi Oswald

The car moves down the long freeway, through the mountains, through the desert, through the long stretches of farmland that go on for seemingly miles, full of sleepy cows interspersed among sleepy towns. As I hear the "put-put-putter" of the engine, and as the AC strains to keep up with the heat, I think about how this car is taking me further and further away from the only place I know. The place where I was grown and raised and watered to sprout into the student doctor I am now becoming. As the miles stretch on, and the closer I am to being 3000 miles away from everything I know and love, I say goodbye to my community. Louder at first and then softer when I know they can no longer hear me, but I say it for my benefit because I believe that when I speak, they will listen, even from far away.

Moving from Seattle, Washington to Charlottesville, Virginia was never the plan for me. But who can control when life calls? We must go where the wind takes us and cope with the losses that may ensue henceforth. We are meant to brave the unknown, we are built by the hardships in our past and when we are ready, we leave the safe places where we have come from. But as I reflect on this experience, I begin to realize that even though this was the first time I have moved far away from my community, this is not my first venture into the world of being physically disconnected from it.

I remember the days before the disconnect. Before the panic buying and the endless Zoom calls, before the two-week quarantine that was going to save the world but didn't. Before we knew what "social distancing" and "6-feet apart" even were, and before the world of never knowing what the bottom half of someone's face looks like. In the days before the world changed, I attended a university-sponsored party hosted by myself and graduate students at the university where I was working as a research scientist. There was laughter and fun, and people were standing close to one another and hugging their friends. Everyone was smiling and life was good. I left that party thinking how lucky I am to have this community of friends. How lucky I am.

Then, a few days later, we learned the world was no longer safe. No one was safe. You could be carrying a virus that may lead to your Grandma's death, and you wouldn't even know it. We became isolated from one another, scared to hurt the ones we love the most. I wasn't able to see my grandparents for months, and talking over Zoom just wasn't the same. There were fights among friends and family members, varying opinions on what is "safe" and what is "necessary." No one knew what they should be doing, what could be done. We tried to live as best we could. While droves of workers transitioned from working in the office to working from home, I continued my hour-long commute to work each day. As a scientist, an essential worker according to the governor, it was up to me to continue working in person with my hands, deep in the biosafety cabinet, hands hidden behind gowns and gloves that were in continuously short supply. It was up to me to coax along the living existence of the cells that were in my care that could maybe help answer questions science has long been searching for, which could maybe create treatments that could help patients in the future. Maybe. If I was lucky. Unfortunately, there was nothing I could do for patients to help them today, which frequently brought up feelings of frustration. My impatience constantly reminded me of why I chose to apply to medical school and follow the path of becoming a physician instead of a scientist, even though I highly value the work of both professions.

However, even though the science marched on, there was no longer any laughter in the lab. There were no more work parties with loud music and all of us crammed together in the tissue culture room having a dance party. Instead, with somber eyes, we recounted the day's new COVID cases and asked each other again when we thought the vaccine would arrive. Our lab policies instructed us to work independently and never closer than 6-feet. We had one-way hallways and daily sign-ins and weekly COVID tests and it was harder than ever to feel close to one another. I ended up teaching the new-hire lab technician techniques through a glass door so we could still see one another and could be closer than 6-feet apart, yet still be protected from the dangers that one of us might have been secretly harboring. Innovation was a daily occurrence and a necessity in this way of life. Months passed, and then a year went by, and eventually, in what seemed like both forever and a blink of an eye at the same time, we had not one type of vaccine, but three different kinds.

Before I left for Charlottesville, once everyone had received their vaccination and before we were all afraid of the Delta variant, I attended an outdoor birthday party with the same students whom I had been at the party with over a year ago. There were hugs and laughter like at the first party, but there were other things present here, too. Nervousness, apprehension. How do I talk to people at a party? Where am I supposed to stand? How long should I stay? When should I arrive? It was like somehow, during our isolation, we forgot what it meant to be human. But as the party continued, we began to remember ourselves again. We remembered ourselves by connecting with one another. Without our community, we cannot live to our fullest potential, and not even Zoom can replicate the feeling of being close to those who lift us up the highest and help us become who we truly are.

Once I arrived in Charlottesville and settled into my new apartment, I prepared to enter medical school with the hope that maybe, just maybe, things would be going back to normal soon. Not the "new" normal that people in positions of power keep repeating over and over again in an effort to increase morale. I mean the real normal, like how it was before a global pandemic ravaged the earth. Before everyone was afraid of hugs and spending time together and knew what mRNA even was. But the gossip about the Delta variant was increasing and the day before school officially started, I received the email stating that yes, masks would be required and not stating that no, there would be no normal for you. At least we could still be together even if we don't know what the other half of each other's face looks like. For whatever reason, at least to me, it seems like the longer we continue living this way, the easier it is to deal with whatever changes come next. But I know that not everyone may feel that way and I try to remember that for others, each wave of disappointment may be even harder to handle than the last.

In the face of such uncertainty and changing times, we must have grace for one another as we attempt to rebuild the foundation of what makes us human. Many of us have had our communities ripped out from under our feet not once, but twice and maybe even more times than that. You cannot know how many pets, people, or places someone has lost along their journey to get to where they are today, and you may not understand how long it may take for them to discover who they are as themselves once they have experienced so much loss. But what you can do is extend that extra smile, the extra encouragement, and the extra love to help someone engage in new communities to not replace, but potentially augment, the ones they have been forced to leave behind. It is only through the strength of togetherness that we can begin to rebuild our humanity.

My Patient, My Teacher

By Lydia Prokosch

As a first-year medical student, in 2018, I was randomly paired with Jack through the University of Virginia Patient Student Partnership program. I was expected to accompany him to medical appointments, familiarize myself with his medical history through the electronic medical record, and help him navigate barriers in his access to care. In turn, he joined the program to teach me what it's like to live with a chronic disease and how to become a patient advocate.

I first met Jack in a coffee shop in Charlottesville, Virginia. He placed a diagram of a heart on the table, and started off our conversation by asking me to identify the names of every anatomical structure on the page. Several weeks later, at a doctor's appointment, Jack's internist pointed to a flickering on the side of his neck – jugular venous distension – a telltale sign that Jack's heart was pumping poorly. These were my first lessons in cardiovascular medicine.

Long before we met, Jack's dream was to become a professor. He graduated with a PhD in business from Columbia University during the Vietnam war, when student enrollment – and thus hiring – were low. Unable to secure a position at an academic institution, he built a successful career in the airplane industry. Jack was known for his friendly demeanor and his dedication to forming connections with colleagues and clients. Over the course of his career, he applied his interest in teaching to mentoring young employees at his firm.

In his forties, Jack met his future wife, Maria. Originally from Cuba, she studied social work and engineering. Maria's first husband had passed away from glioblastoma, a devastating brain tumor. Together, Jack and Maria honored her first husband by supporting cancer research and fundraising for non-profit hospice organizations. Jack became a part of Maria's family, and grew close to her daughter and three grandchildren. He was especially proud of his granddaughter's decision to pursue pediatric intensive care nursing and loved golfing with his grandsons.

Nine months into our partnership, Jack developed shortness of breath walking up a short flight of stairs. When he pressed down on his ankles, his fingers left half-moon imprints. We knew that his cardiovascular function was declining. Over a series of meetings, we sat down and discussed a procedure that his cardiologist recommended. The surgery was risky because like many older adults, Jack had other chronic medical problems and had undergone prior cardiac surgeries. He introduced me to primary literature about the procedure and wrote down a list of pros and cons. We talked about his quality of life and how he wanted to spend his remaining days. He spoke about his enduring love for his wife and grandchildren.

Together with his doctors, Jack decided to proceed with the surgery in August, 2019. His surgeon removed the pacemaker wires that snaked through his tricuspid valve and inserted a prosthetic valve. Although he had several complications, we were cautiously optimistic. A month after the procedure, his surgeon cleared him to play a few holes of golf.

Suddenly, without warning, Jack died five weeks after the procedure. Maria found him in cardiac arrest in his armchair and called the rescue squad. Jack's internist called me to share the news. During the following week, I attended his funeral. I sat next to his surgeon, who cried during the service.

Before each of his surgeries, Jack had written Maria a series of love letters, which she read at his funeral. He told her stories about their early dates. He recalled their car breaking down on a long road trip down South. He explained that he was willing to take risks for the chance of a more functional life. He asked her to think back on their relationship with gratitude.

Several months after his passing, Maria joined the Patient Student Partnership as my new partner. The COVID pandemic started and our in-person visits transitioned to phone calls. She taught me about navigating grief with grace and kindness. In a period of worldwide loss and loneliness, we shared a special connection through remembering Jack's life.

After eighteen months of working together, I recently introduced Maria to a first-year medical student, who will be her new partner through the Patient Student Partnership. I am now seven months away from medical school graduation, and this moment signified my first of many transitions from a student to a resident physician. Even though we are no longer officially partners, Maria and I stay in touch. We still talk about Jack, and we also look to the future – like her granddaughter's aspirations to become a nurse practitioner and my upcoming wedding, which Maria is invited to attend.

Jack and Maria were my first, and most important, patients in medical school. They taught me about love, chronic disease, difficult decision making, death, grief, gratitude, and hope. Over four years, I grew to know them as a couple, and as individuals. The lessons that they shared will stay with me throughout my career and life.

O Positive

By Daniel Bass

This is a work of fiction.

It was 5:47 pm on a Friday and I had a monster of a headache. The score that just appeared on the screen before me after six mind-numbing hours of practice MCAT questions was not the one I had been hoping to see.

Out of the window in front of me, the shimmery aftermath of a brief summer rain clung to the rusty, peeling shutters of the house next door. I tried momentarily to estimate how many minutes I had spent staring blankly at those shutters since moving in six weeks ago but quickly gave up. No more calculations for today. I sat there, staring blankly ahead and contemplating my next move. Under normal circumstances I would probably have plans for the night. Maybe I'd go out with friends, or maybe have some people over to hang out on the balcony of my dilapidated, but nonetheless charming house a few blocks away from campus. None of that would happen tonight. All the cute, wholesome things I envisioned for this summer had evaporated completely four months ago. In case you hadn't heard, there's a virus going around.

I sat another minute longer, watching the light return to the evening sky through the raindrop-covered windowpane and allowed myself a few more moments of self-pity. I then slammed my laptop shut and strutted out of my makeshift study space with a confidence I didn't really feel entitled to. The floorboards groaned beneath my aggravated stomps as I navigated empty rooms to reach the oasis of stained carpet and chipped wallpaper that was my bedroom. I flung myself carelessly onto faded gray sheets and shut my eyes. Momentarily, I allowed longing daydreams of normalcy to fill my consciousness. Friends and fun and big gatherings free of fear and masks and the looming spectre of viral proliferation--blissful pipe dreams from a world I couldn't stop lusting after even though I knew it was long gone.

Emerging from the tantalizing rabbit hole of wishful thinking that never failed to lure forth my idle mind, I snatched up my phone and sent a quick text into our group chat.

"Still on for dinner at the Quad? If we bring a blanket I think it will be dry enough?" I typed.

A few minutes later three little thumbs ups appeared on the message, signifying a decisive, if somewhat passive, concurrence from the quarantine companions with whom I shared nearly every free evening of this strange, depressing summer. The promise of human companionship helped somewhat to lift me out of my MCAT-induced grouchiness and I rolled off the bed with a groan. I pulled on an old tee-shirt and one of the many pairs of blue soccer shorts with my high school insignia emblazoned in embarrassingly large font down the sides. Stepping outside to begin my semi-daily run, I sent a quick reply.

“Perfect! Meet you guys on the steps at 7ish - will bring drinks (smiley face emoji with cowboy hat).”

The air was warm, and the wet pavement smelled inviting as it passed sluggishly beneath my feet. “Green Light” by Lorde spurred me on and I pushed forward down my usual route. I kept the music loud enough that I couldn’t hear my lungs fighting for sufficient oxygen. Before the pandemic, the concept of running voluntarily was utterly laughable, but now, like nearly everything else, my attitude toward the practice had changed. The rage, the sorrow, the sheer unfairness of it all--it seemed to gather in the horrid humidity of that Virginia summer and fall away with every bead of sweat that leapt off my brow.

An hour later I was running a hand through my freshly washed hair and hastily pulling on fresh clothes. The fridge door crashed angrily into the wall like it always did as I wrenched it open to grab the drinks I had promised to provide. I kicked it shut again and headed out the door toward the center of Campus, snatching a surgical mask off the table on my way out the door.

The clouds had finally parted enough for long rays of sun to warm the neatly cut grass on which we lounged. Up above, the light was beginning to fade, and the pink and orange streaks in the summer sky assembled themselves into a warm watercolor sunset. My best friend Jack was sprawled out on the lawn next to me, cackling with his uniquely infectious laughter. Elle and Jasmine had just completed a comprehensive rundown of their respective boy problems which we all found equal parts absurd and hilarious.

“Men are trash,” Elle declared in her waning British accent as we all clinked glasses. “Amen,” I added somewhat slyly.

Jasmine threw me a knowing sideways glance, but Jack, having missed the silent exchange between us, laughed and cheered his agreement.

“We really can be the worst, can’t we?” he joked, looking from me to the girls and back again. For a fleeting second, I thought about doing it, but my ephemeral gumption was quickly replaced by fear.

“Yeah, I guess we can,” I mumbled, “let’s head back, it's getting dark.”

Moments later, we were climbing the endless concrete steps leading up to the girls’ apartment.

“I think when it’s gone in a few months, we’re all going to realize we had COVID without even knowing it,” Elle declared.

“I think that might be a little overly optimistic, Elle,” I replied, somberly.

“Well probably yes, but can’t a girl wish for antibodies,” she replied with a scoff, rolling her notoriously beautiful eyes.

“Well, we could all find out if you wanted to!” Jack offered. “Apparently the Red Cross will do a free antibody test if you donate blood. We can all go together if you guys want!”

Perhaps it was because I had finished one too many drinks, or maybe just because I was a public health major who tended to have these sorts of tidbits primed for injection into casual conversation, but I knew it was a mistake the minute I said it.

"Well, I can't give blood, obviously," I shot back with an instinctual immediacy that I didn't know I had developed.

"What do you mean you can't give blood? You're pre-med. It's not like you're afraid of needles!" Jack replied with a casual chuckle.

It should have been an easy one. There was no reason I couldn't have played it off like the million other moments I had escaped with reflexive dexterity. Maybe I did it intentionally, trapped myself on purpose so I didn't have a choice. Whatever the reason, in that moment I knew my time was up. I felt myself start to choke as a lifetime of white lies burned bright red on the surface of my cheeks. My head was swimming with secret memories that I had never shared with my best friend. The blonde boy who I almost loved a summer ago. The names in my phone that he didn't know about. The nights I had spent slipping in and out of our apartment undetected while Jack and his girlfriend slept soundly on the other side of my wall. All the things I had ever feared would undermine the relationship he always thought we had, the friendship I had cherished above all others. I took a deep breath.

"I mean that I'm not allowed to donate blood." I answered, eyes focused firmly on my shoelaces. A ferocious silence gripped the room. Finally looking up, I stared into Jack's puzzled face with a feeble attempt at nonchalance.

"Jack, there's something I've been meaning to tell you..."

Long after the tearful embrace and cathartic relief – long after that night became a treasured memory of a bygone summer – my mind took me back to that moment, to my unexpected tumble out of the closet. I felt a creeping thread of discontent sewing itself into the fabric of my thoughts. Had I really been forced out of the closet by the fucking Red Cross? Would things have been different if I wasn't so acutely aware of my status as a public health pariah, a policy problem for the powers that be?

For years I had been informed over and over again about my place as a gay man in the history of my own discipline. I knew the history, the justifications, the terminology and the stigmatizing turns of phrase. "High risk group," "dangerous lifestyle choices," "infection potential,"–the archaic niceties danced around the message they were no less effectively conveying. You're dirty. You're dangerous. You're disgusting and risky and we don't want you. "BLOOD NEEDED URGENTLY (faggots need not inquire)". Even in the midst of a public health emergency the message was nothing if not clear.

I had taken enough public health courses to know why the government was repulsed by my erythrocytes. I understood why they grouped me into a pool with drug users and tropical refugees and people who have been around farm animals with mad cow disease. It made no difference to them that even after a lifetime of effort I could not change who I was and who I would be forever. Even in the age of Pride months and legal gay marriage, I am still labeled like a perpetrator by my own profession.

I shut my laptop and stared at the waning sunlight that remained in the sliver of sky that was still visible outside my bedroom window. A lot had changed since that day, but a lot was still the same. I was out and very proud of who I was. But I was also more aware, perhaps less naive. I was "other" and I knew it now. No matter what anyone said I was still being sorted, differentiated, and defined by elements of my existence that generated accusatory questions and social distrust. I had finally come to recognize that no amount of confidence could completely eliminate the insidious, but unmistakable experience of shame.

The sun was gone for good now. It was really starting to get cold outside, and my nameless neighbor had long since pulled closed the rusty, paintless shutters that had been such frequent occupants of my mindless, empty stares. The pride flag on my wall fluttered gently in the torrent of air emanating from the vent overhead. Even in the dark I could make out the chipped paint on the wall that I had hoped would be forever obscured by giant rainbow stripes.

The door opened abruptly, and I clicked my phone off, adjusting my mask over the bridge of my nose.

"Hi there! So good to see you! How'd those MCATs go?" Dr. Rice asked me in his booming, friendly voice.

A few minutes of poking and prodding later and he was wrapping up my yearly physical. If not for his face shield and goggles, it would have felt like any normal doctor's appointment.

"You're an easy case so we can skip most of the usual lifestyle questions I think," he declared matter-of-factly, flipping through a stack of papers as I sat there, gripping the cold brown leather of his ancient exam table. "No risky behaviors of any kind, I'm assuming?"

I shifted my weight uncomfortably and the stiff paper cover crinkled loudly beneath me. "No sir," I replied flatly, "of course not." The handsome, middle-aged internist snapped my chart shut and stood up from his chair, wishing me a Merry Christmas as he did so. On the way out of the exam room he stopped himself, peeking back around the heavy wooden door that was covered top to bottom with the usual public health propaganda.

"Oh, by the way," he offered nonchalantly, "I had a chance to look at your labs in the computer earlier today. No COVID antibodies, but everything else looked totally normal. You've got very healthy blood."

Catch a Vision

By Pamela Tetro

Whither is fled the visionary gleam?
Where is it now, the glory and the dream?
(William Wordsworth 1770-1850)

Many persons when taking on a new challenge say, "keep your eye on the prize" or "jump through the hoops." I like to envision the outcome of a goal which helps me take the necessary small steps along the way. At first glance my theme "Catch a Vision" may seem equivalent to "keep your eye on the prize", but to me it is a softer gaze upon the goal. The idea of a "prize" evokes a sense of competition and a tangible reward.

In my opinion, visions are personal and can be fleeting or longstanding. The information gleaned from the steps along the path can modify or solidify the vision. Some visions may need to be released. My concept of a vision connotes a gentler non-grasping journey to the goal and, if the vision should organically change, there is no judgment. This non-grasping, non-possessiveness concept is called aparigraha in Hindu philosophy. The theme of "Catch a Vision" lightens my spirit while I explore various pathways to the vision. Thus, my journey is flexible.

In the past few years as a family nurse practitioner focused on geriatric care in facilities, I enjoy seeing my elderly patients' quality of life improve -- not only due to a team with skilled geriatricians, but also thanks to the help of the geriatric psychiatrist's skillful assessment, diagnosis, recommendations, and treatments. This experience inspired my vision to obtain an education and skills training in Psych Mental Health to assist frail elders achieve optimum mental health in the setting of challenging health problems. As I explored the practical ways to acquire these skills, my vision expanded to acquiring skills for treating mental health issues in outpatient or inpatient settings, and I am loosening my vision to allow my specialty concentration to evolve as I acquire knowledge in the education process.

This theme of "Catch a Vision" came to me early in life as my family of origin included living with a parent with substance abuse and anger management issues. I was cognizant of the family difficulties at seven years of age and found it helpful to "catch a vision" of the way I wanted my life to play out. Over the years, while living with the situation and beyond, I initially chose to look for lifestyle role models in various families and friends and even some acquaintances that had positive aspects worth exploring/emulating to achieve my vision of a better life. Especially eye-opening was an article in the Portland Press Herald (Maine) that reported eccentric people tended to be the happiest people.

So with soft steps that became louder, I explored and chose my own original steps in the journey toward my vision of a happier healthier life.

My personal experiences and growth have proven to be immensely helpful in connecting with clients while providing professional care in a variety of medical environments; primary care, SNF/LTC/AL and a women's maximum security prison. When I learned about and encountered things like alcoholism, family dynamics and dysfunction, I realized these were not unique to just my family. This served as a source of healing for me. This understanding began to develop when I read Claudia Black's groundbreaking work on adult children of alcoholics which I discovered in the early 1980's. As a result, I attended Adult Children of Alcoholics meetings for a couple years for focused support and improved my coping skills and fleshed out my vision to thrive.

I caught a vision to become a healthcare professional and furthered my education as a first-generation college student completing degrees in Biology and BSN Nursing. After 8 years as a staff RN at various hospitals (including some travel nursing), I wished to make an impact on preventing conditions that lead to hospitalizations and my vision evolved to acquiring nurse practitioner skills in the primary care arena with a MSN, FNP degree from UVA.

While working in primary care, I noticed many diabetic patients were frequently in and out of the office with very high glucose levels and little knowledge of diabetes self-care. These patients were not amenable to a referral to UVA or Martha Jefferson outpatient diabetes self-management programs. Wishing to make a positive impact on their lives, I began training to become a Certified Diabetes Care and Education Specialist (CDCES, previously known as CDE) in 1998, and completed training and certification in 2001. The CDCES training opened an opportunity for me to create a one-to-one diabetes self-management program at Charlottesville Family Medicine in which I fine-tuned skills in diabetes education, motivational interviewing and treatment with the client remaining in the driver's seat to make educated choices about their diabetes management. Fourteen years later, armed with expertise in diabetes care, my next challenge was to accept a newly created role at Augusta Health as the program coordinator for improving inpatient glycemic control. This position was an in-depth practicum on culture changing.

Exploring various spiritual pathways such as Christianity, Hinduism, and Buddhism have always been part of my vision moving me toward more peacefulness and clarity. In 2008, I completed a 200-hour yoga teacher training program as I wanted to know more about quieting and controlling the "monkey mind". My journey continues to evolve as I read and ponder spiritual topics and engage in communities that do the same. I feel no need to dictate anyone else's spiritual journey.

I believe that regular movement to the best of one's ability is important for optimal mental and physical health. My patients appreciate that I call exercise a "dirty word" and that movement and getting the blood flowing is the goal. Patients with poor balance or joint problems are encouraged to use a rocking chair and one-pound weights (vegetable cans) for upper extremities. If movement hurts, we explore modifications to eliminate the discomfort that impedes the joy of movement.

My vision of a balanced life includes regularly touching base with nature. In the past long-distance hiking was a priority. I have fond memories of a five-year midlife running period which culminated in the completion of a half marathon and a sprint triathlon. Gardening in a small, landscaped yard and enjoying creating nutritious meals have helped to keep me grounded as well as humbled by the deer and groundhogs. Currently, I am adapting to the usual aging processes with meditative swimming, gentler yoga, and easier hikes/walking.

The arts are helpful to balance life and support visions whether it be personal talent or appreciation. I have fostered my love of music since childhood. As an adult in MSN/FNP graduate school at UVA, I de-stressed by learning the violin and progressed to an intermediate community orchestra over a span of 10 years (alas no longer r/t a neck injury). I have a theory that one does not have to do anything perfectly to enjoy it thoroughly.

Of course, my personal visions and passions have overlapped, come and gone, often resurging over the years as I have pursued my professional visions. My memories often make me smile. I embrace diversity in my community, country and beyond. It would be a shame if we were all the same. Through travel to foreign countries, my vision has broadened. I do believe that kindness and compassion are good practices to cultivate. Happily, while "catching my visions", I have acquired emotional and physical health tools that also fit in my professional toolbox.

Now, I am embarking on a professional educational journey to become a PsychMentalHealth nurse practitioner.

What is your vision?