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# Making a Meaningful Contribution to Clinical Research

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Making a Meaningful Contribution to Clinical Research

by

Eric Eddy

An undergraduate honors thesis submitted in partial fulfillment of the

requirements for the degree of

Bachelor of Science

in

University Honors

and

Biology

Thesis Adviser

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**Abstract**

Participation in research activities as an undergraduate is a critical part of applying to medical school, or to other similar programs. This research involvement is usually acquired by working in a lab on campus, assisting with either bench or field research. Alternatively involvement in clinical or translational research can be a fitting substitute, but it can be more difficult to be involved on more than a superficial level. It is my assertion that by first assessing ones unique skills, and then seeking an opportunity to apply those skills a more meaningful contribution to the research program can be made.

My own participation with the Critical Care Academic Associates program at OHSU lead to an opportunity to make such a contribution to the Post Intensive Care Syndrome study. The PICS study is a 3 year prospective study and no data will be available for analysis until the study is closed so I have elected to present my thesis as a creative writing project; A memoir of my participation with CCAAP.

**My Rational**

The process of applying to medical school, or any other health professional program, is nearly as complicated as the coursework involved. Everyone knows that grade point average and standardized test scores are important for a successful application, but other facets of the application should be given equal attention, including extra-curricular activities. These extra-curricular activities can be sorted into three categories: Clinical experiences, Volunteering, and Research. Experiences in each serves a specific purpose for the applicant, but the lines between these categories are soft and some experiences may fit into more than one. Clinical experiences help demonstrate to the admissions team that the applicant is familiar with the practice environment and with the physician's role within that environment. Examples of non-clinical volunteering demonstrate to admissions officers that the medical applicant is altruistic.

Lastly, demonstrated research experience shows that the applicant has a level of scientific curiosity, and experience applying the scientific method to problem solving.

While clinical and volunteering experiences are generally viewed as essential to a successful application, the importance of research experience will depend in part on the specific programs that the applicant will be applying to. Some medical schools put a heavy emphasis on research during their curriculum. Duke University and Stanford University for example both require a research thesis from MD students prior to graduation. (Duke, Stanford) This is in stark contrast to the traditional medical school curriculum that consists entirely of clinical rotations during the third and fourth years. Obviously, if applicants have strong interest in conducting research during their training, or as part of their future medical practice, they will be attracted to more research oriented schools. The converse, however, does not necessarily follow: applicants to schools which put more emphasis on training great clinicians, such as Oregon Health Sciences University, nonetheless enjoy many opportunities to do research, even if it is not part of the core curriculum. No matter which medical program they apply to, all pre-health students thus come to realize that some involvement in research will add value to their application. Moreover, most of these students have a genuine interest in doing some research. Most pre-health students seek research experience through a lab on campus, either performing bench or field research, and a smaller proportion seeks involvement in clinical research activities. I chose to pursue clinical research involvement primarily because I hope to include clinical research in my own future practice. Conventional wisdom places bench/field research on a higher tier than clinical research because it allows volunteers to be more directly involved in study design and data analysis.

Based on my own experiences and conversations with my peers the typical experience of a clinical research volunteer is unfulfilling and consists primarily of data entry with occasional superficial interaction with a patient or their family. I assert however that by actively seeking out opportunities to

make a more meaningful contribution their experiences can be more rewarding personally and can contribute more effectively to their application. Finding these opportunities involves 3 steps.

First is taking an inventory of unique skills that you bring to the project. In my own case I had an array of unique skills that most pre-med volunteers do not, due to my prior work experience. I am a skilled mechanic and welder, I have worked in an engineering role on light robotics, I have been responsible for establishing workflows for manufacturing processes, and I have built and maintained databases in the manufacturing environment for example. Most of those skills and experiences had no perceivable application to research in the ICU. There was nothing mechanical that needed to be built or repaired for example, but both my process development experience and my database experience were very valuable to the project and I was able to parley them into a very interesting and challenging project. There are skills and experiences that are unique to every research volunteer that could be put to similar use.

The second step is to identify a need for your special skills on the project. For me it was my process development and database management skills that came of use, as will be explained in the coming pages. The fit here was obvious, but that may not always be the case which is why taking a thorough inventory of your skills is so critical. The third step is to be persistent and advocate for yourself be given the task of filling that need. As you will read, I received some resistance initially but was able to overcome it by being persistent and thorough.

### **Going Beyond Data Entry**

During my sophomore year of college I decided to switch from mechanical engineering to biology and pursue medical school. Having investigated the admissions criteria and recognized the need for research experience I began investigating research programs. A classmate mentioned a program in the Oregon Health Sciences University (OHSU) intensive care unit (ICU) where volunteers participated in

data collection for clinical research. I was very interested in this program. My thinking was that it would provide exposure to the ICU environment along with the desired research exposure of a successful medical school application. I applied to the program, was accepted, and began my training. Before we were allowed to begin collecting data we received about 20 hours of training from the research coordinator. This training included patient privacy training, instruction on the use of the electronic medical records system (EPIC), the database system we would be entering the data into, basic training in the history of critical care medicine, as well as in the studies we would be helping with.

This history of critical care medicine is worth noting in brief because it explains the need for the study I would participate in. During my initial training I learned that the modern intensive care unit (ICU) derives from the unit established by Dr. Bjørn Aage Ibsen in Copenhagen, Denmark in 1953. Ibsen's concept for his unit was fairly simple: maintain sanitary conditions, keep patients sedated to allow their bodies to heal, and manage their breathing with mechanical ventilation as needed (Pincock). Mechanical ventilation became the defining characteristic of intensive care units. Early "Iron Lung" type ventilators were negative pressure devices where patients were placed in a large cylinder with only their heads remaining outside. As the air was drawn from the chamber, creating a low pressure zone, air would rush into the patient's lungs to fill the void. When the vacuum was released, the air would exit. In the late 1950's and early 1960's, improvements in positive pressure ventilation devices led to their becoming the standard for ICU care. (Bahns) The negative pressure devices were minimally invasive, allowing the patient to remain conscious, and had been ideal for polio patients who suffered from respiratory paralysis; but they were physically large and prevented caregivers access to most of the patient's body. On the other hand, positive pressure ventilation is much more invasive; it requires a tube to be inserted into the patient's airway and sealed to their trachea, known as intubation. Intubated patients must be sedated both for comfort and to inhibit their own respiratory drive. The key benefit of positive pressure ventilation is that it allows access to the patient's body, facilitating

procedures and other modes of treatment which would be impossible with a patient in an iron lung. Positive pressure ventilation via tracheal intubation or tracheostomy tube has been the standard in intensive care medicine since the 1960's, and pulmonology and critical care medicine have been tightly related ever since. (Takrouri)

When my training was completed there were three ongoing studies that the group was assisting with. The first was the Stop Hyponatremia use Metolazone (SHUM) trial: a study evaluating the diuretic Metolazone and its effects on sodium depletion (hyponatremia) in ICU patients. My involvement in this project was simply to flag intubated patients in our database; the critical care fellows then made the decision to include the patient in the study or not. The second project was the development of a Northwest Regional Sepsis Database. For this project we screened every patient in the 4 adult ICUs at OHSU and determined if they fit the criteria for sepsis. This was accomplished by digging through the patients' electronic charts in EPIC and then entering their identifying information into a spreadsheet. Again, the critical care fellows handled the entering of the data in to the database after verifying our screening. The final project was a study of the effect of intensive insulin therapy on the mortality and morbidity of ICU patients. This was the project with the most direct volunteer involvement. For this study the volunteers first screened the electronic charts of every patient in the four adult ICUs to determine if they met the study criteria. We then entered all of the required data for each patient into the REDCap database for the study. REDCap stands for "Research Electronic Data Capture" and is database management software designed and maintained by Vanderbilt University specifically to support clinical and translational research studies. The collected data was then verified by experienced volunteers and eventually analyzed by the research team with help from biostatisticians at the conclusion of the study.

### **Proving Myself: The ITT Study**

My greatest involvement with these three studies was with the Intensive Insulin Therapy (IIT) study. For the first year of work with CCAAP my involvement in the IIT study was limited to data collection and verification, just like any other volunteer. The study was interesting to me as I was not aware of the effects of long term hospitalization and the concept of stress hyperglycemia, but this novelty quickly faded and the work became very mundane. There were still interesting moments throughout the shift, but most of these were products of the environment rather than the work itself. We were working either on the ICU floor or in the physician work room, which meant that while we were doing data collection we were also able, and actively encouraged, to observe patient care activities and listen in on physician discussion of treatment plans and related issues. Additionally we were encouraged to observe any procedures that were performed on the unit during our shifts.

One of my most meaningful memories of this time was a conversation amongst a group of physicians in the work room. The ICU attending, several of the ICU residents, and a representative from the palliative care team were discussing the end of life care of a patient one evening. The patient was intubated, and it was the belief of the care team that she would almost certainly not survive to discharge, having had multiple arrests and resuscitations in the days prior. She was able to communicate, but obviously could not speak due to the intubation. During an exam the patient had seemed to indicate that she did not wish to continue receiving invasive measures to continue her life. Later during a meeting with the patient's family to discuss the future course of her care the family had been adamant that the physicians "do everything in their power" to keep her alive. The emotions of the care team were thinly veiled in this candid discussion, away from the eyes of patients and family. They were clearly frustrated and saddened by the situation, which is why the palliative care provider was called to consult. Ultimately the decision was made to stay the course with the patient, who expired a few days later. It was the words of the palliative care provider that most stuck with me. When asked



how he approached these decisions he said that he used “The Oregonian Rule.” Essentially he asked himself if he could justify his decision to go against the will of the family if they decided to call The Oregonian and complain.

I was also able to observe several procedures on the unit; the placement of central lines, bronchoscopy, intubation, extubation, and cardiopulmonary resuscitation. These experiences more than made up for the banal nature of the work, but I still felt that I could be contributing more. Discussion with my compatriots, both within CCAAP and in similar programs, confirmed that this was a common feeling. While we recognized the importance of the work we were doing, and were excited to be a part of projects that could help to define the care of patients for years to come, almost nobody that I spoke with actually enjoyed the work itself. This was not true of my friends who were participating in bench and field research. They were very excited about their work, and some even had small projects of their own to work on in the labs. That was the experience I wanted, but I wanted to do it in a clinical setting where I would be practicing in the future.

In the spring of 2014 the enrollment phase of the ITT study ended and our focus shifted to completing the backlog of data entry accumulated over the previous year. Shortly after, our research coordinator realized that there had been an inconsistency in the data collection process. One of the enrollment requirements for the study when it was established required a minimum of 8 hours of insulin therapy on the first study day. If 8 hours of insulin therapy did not take place that day would be excluded and the second day of treatment would become the first study day. Unfortunately, however, this rule had not been followed for several patients, and owing to the design of the database correcting for these oversights was not a simple task. Initially it was believed that to correct the errors each of these records would have to be re-entered from scratch and re-verified. This would have meant hundreds of hours of work being discarded and replicated. I was confident that I could correct this issue without compromising the integrity of the data, if I could get access to the database. Prior to beginning

my college career I had worked for many years in the electronics industry at jobs ranging from manual assembly of circuit boards to engineering level positions. One of these jobs had been as the manufacturing engineer for an automated electronics production group. During that time I was responsible for the implementation, and subsequent management, of an automated quality control database for the company. I knew that this experience would give me the skills to decipher the database and the understanding of data integrity to make the changes without introducing errors.

I contacted the research coordinator, Kelsey, and set up a meeting with her to discuss my ideas for correcting the entry errors. Kelsey was aware of the problem and her initial response was to fix it through brute force, but after I explained my past experience with database management she agreed to give me access to the database to do some testing. The layout of the database was not what I was used to, but it was easily deciphered. I was able to develop a method for “shifting” the insulin therapy data into the correct position while preserving the integrity of the data. In all, it took 8 hours including testing to develop and document the process. I set a follow-up meeting with Kelsey to review my results and implement the plan. Over the next several months my primary task was correcting these errors in entry of the insulin therapy data as the other volunteers found them. Although we did not track the number of records which required correction, but there is little doubt that there were hundreds of hours saved.

Because of my performance on this project, and my new familiarity with the inner workings of REDCap and the IIT database, my next project was to work with Andrew, a graduating MD/MPH student who was using the IIT data for his MPH Thesis. My specific role was to help him format the data for use in the statistical software he was using to analyze the data. During my involvement in the IIT project I had also been keeping an eye out for a topic I could use for my honors thesis. Andrew had been planning to analyze all of the data in the study to determine the effects of the various protocols on mortality and morbidity. I had been considering a much smaller scoped analysis of the data, simply looking at the effects of the newest protocol in just one of the ICUs. I had been given tentative approval

to do so, but on the condition that I helped Andrew with his project first. I worked intermittently with Andrew for about 4 weeks, mostly helping him with access to the database and understanding the format of the data once downloaded. The database had been designed such that each participant's data occupied multiple lines in the downloaded data set rather than a single row. This decision made sense at the time, as the duration of each patient's stay was variable, but later it greatly complicated the analysis phase of the study. Each patient's data needed to be "flattened" prior to analysis. Our initial plan was to do this manually, but that would be very time consuming and was likely to be error prone. Thankfully the MPH student was able to automate this process within the analysis software using the study participant ID number as a reference. Ultimately the study Andrew had planned was not statistically viable due to the quality and quantity of the data. Andrew decided to instead limit his study to the most recent data, the data collected in REDCap, and to compare just the most recent IIT protocol to the prior two. This less ambitious study was almost identical to the analysis I had planned, which left me without a viable angle to study the IIT data. Luckily, the new post intensive care syndrome (PICS) study was just launching and there was a need for someone with REDCap experience to configure the database.

### **The PICS Study**

I was initially reluctant to take on the task of configuring the database for the PICS study. I was in the middle of my medical school application cycle and was attempting to wrap up my current commitments rather than taking on new ones, and I was unsure if this project would qualify as a topic for my PSU honors thesis. I accepted the task tentatively, on the condition that it would meet the thesis requirements, and scheduled an appointment with the professor leading my thesis orientation seminar to discuss the matter. My concept was met with excitement and approval by my thesis advisor at PSU, and I was given the green light to move forward with the plan. Before I could begin, however, there were some logistical hoops that needed to be jumped, particularly because the study involved human

subjects. Any research involving human subjects is required to receive approval from the Institutional Review Board (IRB) and anyone involved in the administration of the study must be cleared as well to ensure that there are no conflicts of interest. The PICS study had received preliminary IRB approval but was still undergoing some revision at the time my involvement began and Hannah, our new research coordinator, elected to wait until that process was completed before I began on the database. The IRB approval process is fairly straight forward, but can be time consuming. A committee reviews each proposal to ensure that adequate precautions are taken to minimize risk to patients and ensure adequately informed consent. It was several months before I was finally given final approval to begin configuring the database, but that time was not wasted. I was able to use this time to learn more about the history of PICS and its treatments.

### **Intensive Care Medicine and Post Intensive Care Syndrome**

Today with advances in medication and equipment the intensivist (a physician who specializes in critical care medicine) is able to take control of nearly all of the basic functions of the body. As previously discussed, the patient's breathing can be taken over by a respirator. The physician can also raise and lower blood pressure as needed with medication, and regulate the heart rate with internal or external pacemakers. Food can be delivered to the stomach via a nasogastric tube, or infused directly into the blood stream through a process called total parenteral nutrition (TPN). There are catheters for the urinary tract and for the rectum to aid in the management of waste products; and, in the event of kidney failure, dialysis can filter metabolic wastes out of the blood. All of these advances have resulted in a monumental increase in the number of patients surviving to ICU discharge, particularly patients with severe conditions that require longer stays to resolve. Today, it is not uncommon for patients to survive stays of 30 days or more in the ICU and, following rehabilitation, return to a their previous level of activity. These long periods of hospitalization are not without their consequences however; the body relies on being in motion for many of its functions and while sedentary muscles, joints, and even bones

can quickly atrophy. Additionally, there are many psychological effects which are common to patients following prolonged hospitalizations. (SCCM) This collection of symptoms, which is common to patients following a prolonged ICU stay, has been given the name Post Intensive Care Syndrome (PICS). The Society of Critical Care Medicine formally adopted the term during its national conference in 2012. At that time it was established that there was a lack of awareness of as well as a need for an evidence based medicine method to manage PICS.

### **Post Intensive Care Syndrome Literature Review**

Post Intensive Care Syndrome (PICS) was first characterized in the early 1960s shortly after the ICU became commonplace in hospitals around the country. The earliest mention of the term “Intensive Care Syndrome” that I was able to identify was from a paper by Dr. F.P. McKeegney published in the Connecticut Journal of Medicine in 1966, but there were several other papers in the late 1950’s and early 1960’s which described similar issues such as post-surgical delirium and post-admission weakness. The Society of Critical Care Medicine officially defined PICS at a meeting in 2012 and stated that it consists of 3 categories of symptoms: ICU-acquired weakness, cognitive dysfunction, and other mental health problems. The first two categories are fairly self-explanatory. The third category, other mental health problems, however is more amorphous and includes such symptoms as anxiety, false memories, and post-traumatic stress disorder. (SCCM) In 2008, a study by Dr. Weinert examining the effects of wakefulness during mechanical ventilation improved mortality and morbidity rates, but with an increase in negative long term psychological effects. The study went on to explain that the correlation between wakefulness and psychological effects was stronger than that of either ICU length of stay or exposure to sedatives. This supports the assertion that the recent trend in decreased sedation levels are a significant contributor to the increased prevalence of PICS symptoms.

ICU acquired weakness is the most easily recognized and explained of the PICS symptom categories. It is intuitively obvious that long periods of time spent immobile will lead to muscle wasting.

What is less intuitive is that even passive range of motion therapy can reduce the atrophy and speed recovery. A 2013 study published in the journal *Critical Care Medicine* discussed the findings at three large tertiary care centers across the country where early mobility was implemented. At all 3 centers it was shown that early and frequent mobility therapy, even passive motion therapy, resulted in shorter stays with fewer days spent intubated. The addition of the mobility therapy was also found to not increase cost for the patient or the hospital. One surprising finding was from the paper published by Morris et. al. in 2008 which showed that increased mobility therapy also reduced the prevalence of acute respiratory distress syndrome (ARDS) leading to fewer and shorter intubations for patients.

“Cognitive Dysfunction” refers to permanent loss of mental faculties, in this case as a result of the patient’s illness and/or their stay in the ICU. In 2001, Ely published a study in *Critical Care Medicine*, which established a standard for the evaluation of delirium. These standards are still used in ICUs across the country. The leading theory regarding long term ICU related cognitive dysfunction is that it is a direct result of episodes of delirium while in the ICU. It has been shown that both the frequency and duration of delirium episodes during an ICU stay are related to the level of dysfunction. (Pandharipande) It has also been shown that infection, particularly urinary tract infections (UTIs), can contribute to episodes of delirium during an ICU stay. Catheterization has long been known to be a contributing factor with regard to UTIs and it has been theorized that improper securing and routing of the drainage tube could be the cause. A study by Ely et. al. in 2008 showed no correlation between catheter drain routing and frequency of catheter induced UTIs.

The most widely studied aspect of mental health issues following ICU stays is PTSD. A study of 80 patients in 2001 Scragg et. al. showed that nearly half experienced anxiety following their ICU admission and over one in three had symptoms of PTSD. This correlates well to more recent studies by Jones which showed that PTSD was frequently experienced by both patients (2004) and their families (2007). Jones then chose to pursue the task of finding a preventative measure which could be taken in

the ICU. One measure that they tested, with good results, was the use of ICU diaries. In 2010 they published a paper showing that the use of ICU diaries, kept by the patient during their stay, or by family and staff if they were unable, resulted in a significant reduction in both the severity and duration of ICU induced PTSD.

The incorporation of all of these factors has led to the development of the ABCDE bundle as described by Balas et. al. in Critical Care medicine in 2014. This bundle is designed to address all aspects of PICS with preventative measures during the patient stay. One aspect that the ABCDE bundle does not address in depth however is how to address patient anxiety and PTSD following discharge.

### **The OHSU PICS study**

Our study would be implementing several protocols in the medical ICU (MICU) at OHSU, each of which is intended to address a specific aspect of PICS. The suite of therapies is referred to as the ABCDEF bundle. Let me unpack the meaning of the letters. ABC stands for “Awakening Breathing, Coordination” of care and choice of sedation. Patients who meet study criteria will receive multiple paired spontaneous awakening and breathing trials daily with the goal of weaning the patient off sedation and ventilation as quickly as possible. D stand for “Delirium and Diaries.” Patients will receive delirium screening twice daily using the CAM-ICU algorithm and ICU diaries, which include educational material and a rehabilitation manual, will be provided to patients and their families to help mitigate the cognitive impact of the ICU stay. E stands for “Early Mobility.” It is crucial to get the patient moving as much as they are capable as soon as possible. This early mobility therapy will cover a spectrum from passive range of motion (PROM) where the patient’s limbs are being moved by hospital staff through walking with assistance outside the room on the unit. CCAAP volunteers, under the supervision of the MICU staff, will perform passive range of motion while all active exercises will be monitored directly by the staff. Lastly, F stands for “Family education and follow-up.” Much of the family education will be provided in the PICS education and rehabilitation manual along with the ICU diary. Follow-up will

consist of telephone surveys at 3, 6, and 12-month intervals as well as a physical examination at 3-months post discharge in the PICS clinic. Patients will also receive referrals to physical therapy and psychiatric care as appropriate.

There are several primary and secondary measures, which will be collected and tracked in the database I designed. These include the patient's score on various surveys, length of stay in the ICU and in the hospital, lower extremity strength at discharge, and incidence of psychological or cognitive impairment. Upon admission to the ICU various patient demographic information will be collected, and while the patient remains in the ICU data will be collected each day. This daily data will consist of the patient's ventilator status, the number of spontaneous awakening and breathing attempts, their CAM ICU score (indicator of delirium), and the number and type of mobility sessions the patient received. Additionally the date that the patient, or their family, received the ICU diary will be collected, and the thickness of the patient's rectus femoris muscle will be measured on ICU day 1, 3, 5, 7, and 10. It is not uncommon for patients to be discharged to a step-down unit or even to a standard medical/surgical floor as their condition improves, but as the patients we are tracking are the "sickest of the sick" their condition can also easily worsen after transfer leading to a return to the ICU. The database must take this possibility into account and have the flexibility to accommodate these complex admission cycles. When the patient is eventually discharged from the hospital, several specific measures must be taken so that their post-hospital condition can be evaluated. These discharge measures include a measurement of their physical and mental capabilities, and information on where they will be discharged to (home with family, or to a skilled nursing facility for example) and how to contact them. Lastly, the database will track the individual answers to the telephone surveys and the patient's score on each survey; a scan of the form filled out by the fellow during the survey will be uploaded to the database to act as a backup of the information.



## **Building the Database**

Before I began configuring the database, Hannah and I felt that it would be prudent for me to take the short (4 hour) REDCap training class, which is hosted by the Oregon Clinical and Translational Research Institute (OCTRI). This class is specifically designed for people who are responsible for creating and maintaining REDCap databases for research being performed at OHSU. OCTRI is also responsible for quality checking the databases produced to ensure that privacy policies are implemented properly. The class was helpful, and well put together, but was aimed more at people who did not have much experience with database configuration or management. That being said I did pickup many useful tips and tricks, which I was able to put to good use during the configuration of the database. After completing the class, I again met with Hannah and we put together a plan for the project. I would work a 4 hour shift every Monday morning. There is a work room just down the hall from Hanna's office that has been set aside for research work. I was given copies of the study documentation, but I was not allowed to take them home with me. I spent my first shift working on the database by reading the documentation and compiling a list of variables that would need to be collected for each patient. I built an Excel spreadsheet to keep track of them and created a folder on the CCAAP shared drive to store my working files in. The database itself is a live document saved on a remote server and accessed through the OHSU intranet, but any other files I was using to keep notes in or any exports from the database would have to be saved separately.

The first active configuration step was to map out the flow of the database. One key consideration here was the desire to keep the data for each patient on a single line when the database was exported for analysis. This was a significant issue during the analysis phase of the IIT study data. In the IIT database the daily data for each patient received its own line in the exported file, as did the demographic information, admission data, and discharge data. Before analysis this data had to be "flattened" to be compatible with the statistical software being used. This format is a byproduct of a

feature in REDCap which allows the recycling of a single form as a patient's course progresses. It is a great feature for the database designer, and for the data-entry team, but there is very little value added once the analysis hurdle it creates is considered. In my database the daily data would be appended to a single form for the ICU admission, which is configured to expand as the patient's stay lengthens. There are three identical forms for collecting the in-hospital data and each one will allow for up-to 24 days worth of data. Continuous stays of more than 24 days will be collected using two of the 3 forms and notes indicating such will be made in the appropriate fields on the forms. History shows that this should allow us to capture all of the data needed while still maintaining a flat data output which should make analysis run more smoothly.

Once a plan was established the coding of the database began. There would be a total of eight forms for data collection, although they would not all be used for every patient. I started with the hospital admission data form because it was very straightforward. All of the hospital admission data will be collected for every patient and it is all easily acquired from the electronic medical record (EPIC). Similarly the hospital discharge data was initially consistent from patient to patient. The three forms for collecting the in-hospital measures would all be nearly identical and would expand as the patient's ICU stay lengthened through conditional formatting. Conditional formatting allows existing fields on a form to be hidden or revealed based on the data entered into other fields. For the in hospital measures form only the first day's data is available for entry. Under day 2 there is one yes or no question available: "Still MICU patient?" If the volunteer answers 'no' then the form remains small and the volunteer can enter the ICU discharge data. If they answer 'yes' then the data for day 2 can be entered and a similar yes/no prompt for day three becomes visible. This pattern continues through day 24. At the end of the form is the option to indicate where the patient was discharged to; the hospital floor, SNF, Home, or deceased. There is also a notes field, which can be used to indicate that the patient is still a MICU patient and that the data collection is continued on form two or three as appropriate. To speed the

coding I built the first form and copied it to make the other two. REDCap does not have the functionality to copy a form directly, but it does allow you to manipulate the database code in Excel through the 'data dictionary.' With the data dictionary I was able to copy all of the variables associated with the first in-hospital data form and create the other two. This did require some manual manipulation; each variable had to be re-named to be unique and all of the conditional formatting had to be modified to reflect the appropriate variable names, but this was still much quicker than building the forms from scratch and had less chance of errors.

After creating the in-hospital data collection forms it was time to create the phone interview forms. There were a few formatting options for the function of the form, depending on how the data was to be entered. We knew that the research fellows would be conducting the phone interviews so my initial assumption was that they would simply open REDCap and enter the data directly as the interview progressed. Based on this assumption I constructed the database form to act as a script for the phone interview. Unfortunately when this idea was presented to the fellows they rejected the idea, preferring to record the interview on paper and then have it transcribed into the database by volunteers. While this is a less efficient strategy overall, it will be more efficient for the fellows themselves, and volunteer labor is plentiful. We considered simply entering the survey scores into the database and attaching a scan of the paper survey form, but in the end being able to analyze the data based on specific answers to survey questions seemed like it might be valuable. All three of the phone interviews are the same and consist of two surveys; one addressing the economic impact of their illness and the other assessing how the patient feels their outcome has progressed. Again I built the first form and copied it using the data dictionary feature.

The final form that I needed to create was for the 90 day PICS clinic exam. For this exam there will be a repeat scan of the rectus femoris via ultrasound along with repeats of the assessments that were performed at hospital discharge. In this case the granularity was not required so the scored will be

entered into the database and the forms will be scanned and uploaded as appropriate. At this point the construction of the database was initially complete. I set an appointment with Hannah to review the database and make any changes she felt were needed. One idea we discussed was the use of REDCap's survey feature to enable the fellows to enter the data directly during the telephone interviews. This required me to attend a second training class specific to the survey function. After this class I configured the phone survey forms to behave as surveys. The thinking was that the database could handle the scheduling of the phone surveys while eliminating the extra labor needed to transcribe the data into the database from the paper forms. After some testing, however, we found that the system did not have the functionality that we had hoped. The system is really designed for the form to be completed by the patient directly and as such it does not allow for multiple recipients, as we would have in this case. While the idea was sound it did not translate to practice and was discarded.

Along with the attempt at using the survey functionality there were very few corrections that needed to be made following my meeting with Hannah. I added some calculated fields to the in-hospital data forms to help prevent missing data, and to the discharge information form to simplify the analysis phase. I also disabled the survey functionality for the telephone interview forms. At this point the database was ready for some thorough testing, and release to production. There may be small adjustments that need to be made after the database is used in production as unusual circumstances arise. This is fairly normal for any new software application; one can never anticipate every situation during testing. I had initially planned on writing the work instructions for the volunteers entering the data but due to time constraints, those instructions will be written by the Hannah or by another volunteer.

## Conclusion

Conventional wisdom tells medical school applicants that research involvement is important, and that their research contribution needs to be meaningful. For most people the indication that their input to a project was meaningful is their inclusion as a co-author on the publication. Being listed as a co-author is also very easy to demonstrate to the decision makers; there is a written record of the publication that can usually be found quickly and easily online. There are many factors, however, that make this unlikely for undergraduates involved in clinical research.

For example, many clinical research studies, including those discussed here, are several years in length. For most undergraduate pre-med students the timeline makes it unlikely that a study they contribute to will reach publication prior to their application. The fact that clinical research involves human subjects and tends to be conducted by physicians complicates this timeline. There are a limited number of roles on these projects that are suitable for undergraduates, most of which are essentially data entry roles. In my experience there are other opportunities for deeper more meaningful involvement, as I have demonstrated here. The key to filling these roles is three-fold; first one must identify her/his special skills, then he/she must identify a need for those special skills, and lastly she/he must be persistent in seeking the opportunity to fill that need. Doing all this of course takes time, again making it unlikely to be published prior to application. In my own conversations with other applicants I met only one who had a publication prior to application, and she was an older applicant who had been working in a lab for several years prior to applying.

Ultimately I can only speak to my own experiences. During my application cycle my involvement with CCAAP proved to be very valuable. I placed my involvement in the program at the forefront of my application. It was a topic of conversation in every one-on-one interview that I had, and based on comments from interviewers it was also the source of what I believe was one of my strongest letters of

recommendation. Interestingly my involvement in the PICS study did not begin until after I had begun interviewing, and my application information was all based off of my IIT study involvement. I believe that my PICS study involvement would have been even more valuable if it had launched earlier. The PICS study being a 2-3 year prospective study will not have any usable data for quite some time, which is why I have presented this thesis as a memoir rather than as a scientific paper. I will be attending OHSU for medical school and may continue my involvement in the project if time permits.

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