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Quality Management: A Global Case Study in Organ Transplantation

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Quality Management in a clinical research setting: A global case-study of Organ Transplantation

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Abstract

Every year the US and European countries face an epidemic of organ failure from a multitude of reasons: cancer, genetic predisposition, exposure to harmful chemicals in home or surrounding areas or through drinking, drugs and smoking. Another problem faced, is the ratio of organ donors to organ recipients. Over 121,000 patients are on the waiting for an organ transplant, and a fraction of those waiting will die because of time. The Hanover Medical school and department of quality management, have created an integrated approach to organ transplant avenues. Quality management is a systematic guide for organ transplantation that allows all clinical trials to follow a standard operating procedure and protocol. This paper will talk about the use of integrated pathways in transplantation management in US/EU transplant centers. It will also discuss how quality management plays an intricate/necessary role in ensuring all clinical trials are efficient in organ transplantation and can meet the necessary demands of saving lives, while improving outcomes of transplanting vital organs. I will also discuss the gaps present in clinical research and the current research that's being down to enhance the field of organ transplantation. The role of quality management is to ensure that all studies are performed with proper efficacy, high ethical standards, and contain a set of clear standard operating procedures and protocols for each clinical trial.

Key words: Clinical management, QMS, organ transplant

Problems with Clinical Research

This summer I participating in a clinical research program through the University of Hochschule Hanover of Applied Science and art in Germany. To complete my 300/hr. internship, I interned through the department of Quality management at the Hanover Medical school. The U.S public health problems that are prevalent are: Accurate assessments of alloimmunity, simultaneous dissemination of assays to the transplant community, which means making the screening process more thorough for detection of disease, international exchange of data to optimize safety and efficacy leading to increased success within the clinical pathways of organ transplantation, and uncovering the unmet needs of patient's pre-transplantation, peri-transplantation & post transplantation. Through the internship, I focused on the use of Clinical Pathways in organ transplantation management in the U.S./EU.
Every day on average, 22 people die while waiting for an organ transplant in the U.S and European countries. (UNOS, 2016).

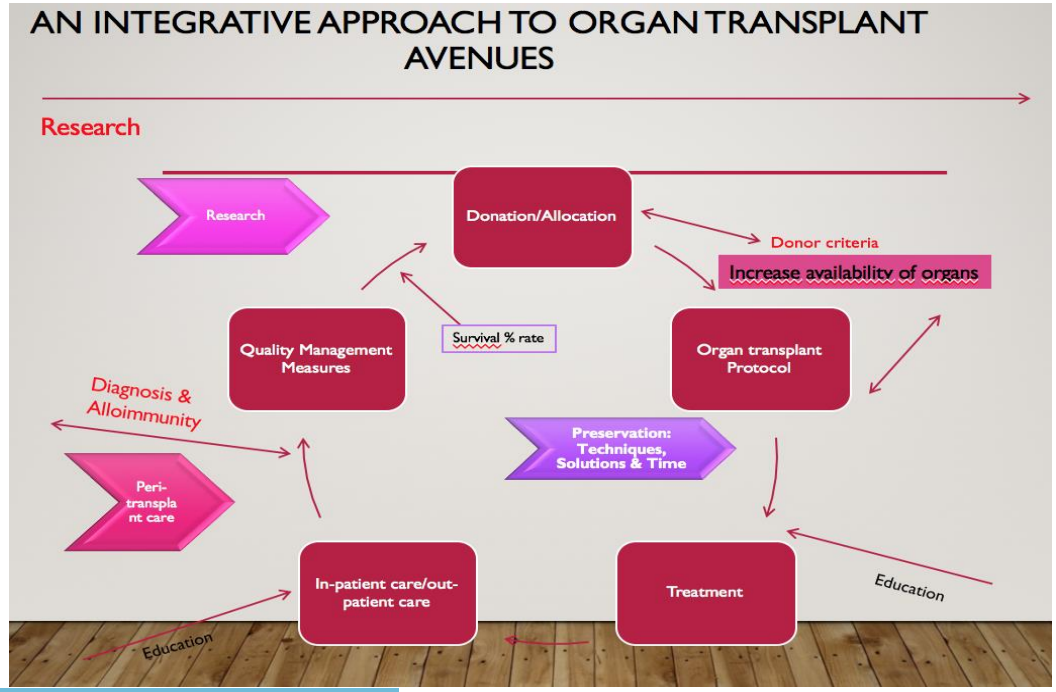
The project I worked on was to see what clinical pathways are established for organ transplant management in the US/EU transplant centers. The purpose was to find connections in how countries acquire/transport internal organs to organ recipients around the world, and how the quality management can improve utilizing quality assurance and quality control within the clinical setting. The public health problem is organ transplantation and the continuous gap that's increasing between organ supply and demand in the U.S and European countries (EU). In 2014, there were 39,973 organ transplants performed in the U.S with a 5% increase from 2014 to 2015 (HRSA, 2015). There was a total of approximately 114,690 organ transplants worldwide, of which 30.9% per 1000 transplants occurred in the U.S. and ≥25% in the European Union (EU) (HRSA, 2016). The World Health Organization (WHO) has issued a resolution and guiding principles in consideration thereof, particularly noting the following challenges: The shortage of available organs has not only prompted many countries to develop procedures and systems to increase supply but has also stimulated commercial traffic in human organs, particularly from living donors who are unrelated to recipients. The evidence of such

commerce, along with the related traffic in human beings, has become clearer in recent decades. Moreover, the growing ease of international communication and travel has led many patients to travel abroad to medical centers that advertise their ability to perform transplants and to supply donor organs for a single, inclusive charge (WHO, 2010). Second, there is a current awareness of the growing magnitude and utility of human cell, tissue and organ transplantation for a wide range of conditions in low-resource as well as high-resource countries; A third challenge is to ensure the safety, efficacy and ethical standards are followed for each patient and future donor. The fourth challenge was stated in the resolutions WHA40.13 and WHA42.5 and first expressed the Health Assembly's concern over commercial trade in organs and the need for global standards for transplantation. Lastly, among the most pressing challenges for population health researchers and clinicians is the accurate assessment of alloimmunity and simultaneous dissemination of assays to the transplant community are essential for post-transplantation surveillance and international exchange of data to optimize safety and efficacy (WHO,2010).

In response to this, a number of initiatives have been proposed, including the potential establishment of a global virtual laboratory, the assessment of outcomes post-transplantation, and navigation of ethical and legal considerations. Developing a GVL would mean disseminating detailed and rigorous protocols for the monitoring of alloimmune responses. It aims to initiate steps at making standardized testing methods and expertise more accessible to the global transplant research community conducting clinical trials (Geissler, Tullius, Chong, 2015). This will be able to implement novel transplantation strategies that can improve long-term outcomes (one of our current most challenging issues).

An integrative approach to organ transplantation

A quality management system (QMS) is a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives. A QMS helps coordinate and direct clinical trial activities to meet patients and regulatory requirements of that hospital and improve its effectiveness and efficiency on a continuous basis. The department of quality management in Hanover Germany, created an avenue for an integrative approach to organ transplantation and how it can increase success in organ treatment. Their purpose is reducing loss of organs, increase long-term success/results and increase the amount of time an organ be en route to a patient in need (ASQ, 2015). The diagram below shows an integrative approach to organ transplant avenues for organ transplantation, as well as, how other areas can contribute to the success of 1 of 5 main branches.



Quality management allows continuous improvement in quality control, as well as, quality assurance of all clinical trials performed in Germany. Germany has begun creating an integrative approach using quality management control within organ transplantation systems. The QMS helps provide a systematic guide in the development of a robust system for reporting, investigating and resolving all errors, accidents, adverse events and biological product deviations and complaints. This will ensure the "process" that is at fault or having errors be fixed because it will be one of the most important aspects of safety in transplantation. Clinical research will have more opportunities in achieving optimal success with having quality management oversight in all avenues (ASQ,2015).

One of the benefits of developing and implementing a QMP includes developing proactive communication among clinical trial team members. This benefits clinical trial teams by encouraging early identification and resolution of clinical trial problems and concerns. Implementing a Clinical Trial QMP can also encourage conformity with Standard Operating Procedure, Good Clinical Practice (GCP), Good Laboratory Practice, and UCSF policies and procedures. This leads to an overall reduction in external (Sponsor, FDA) and internal (UCSF) data queries, and helps reduce clinical trial closeout time (UCSF, 2015). All transplant related procedures are subject to continuous review and improvement. If certain parts of the services provided by the transplant center are to be amended significantly or a new field of procedure are developed, a new plan of development should be compiled and released by the medical program director. This is the purpose of why quality management is a part of clinical research trials; it will provide access to more reliable data/statistics, ensure ethical protocols are followed, monitor and measure the process and service

Another important aspect while working on integrative pathways in organ transplantation, is the transportation and allocation for each organ. The purpose of this project was to find ways to increase the preservation time of each organ by creating new techniques to store/transfer. Organ preservation remains an important contributing factor to graft and patient outcomes (Latchana, Peck, Whitson, Henry, 2015). Today's Current Standard of Care: The Picnic Cooler vs. OTS' Revolutionary Technology: The LifeCradle® Heart Perfusion System (OTS, 2012). Both techniques are in use and under review of which one will be able to preserve

the organ the longest, which will give more flexibility with allocation of the organ. Focusing on preservation solutions represents one potential avenue to improve patient and graft outcomes in transplantation and may be an effective strategy to decrease healthcare costs associated with transplantation (Latchana, Peck, Whitson, Henry, 2015).

Shown below is a table that provides an example of treatment avenues and what qualifies a patient to receive an organ transplant (i.e. diagnosis), and how to measure outcomes/patient survival. Measuring outcomes is extremely essential to measuring success of treatment post-transplantation. Organ failure typically begins one-year post-operation, which is why quality management control is an important avenue in organ transplant research.

Organs	Dx receiving transplant	Tolerance: measuring outcomes	In/out PT survival	% of transplants done	U.S or EU
Heart	CHD, CAD, HF, PHV, HD	Pre, peri, post trasnplant protocols	Specific for each site of transplant	2804	U.S
Lung	**Bilateral Lung Transplant;** Cystic fibrosis, Bronchiectasis, Pulmonary hypertension,Emphysema Pulmonary fibrosis (idoiopathic or secondary to scleroderma or other disease states) **Single Lung Transplant:** Emphysema, Pulmonary fibrosis (idoiopathic or secondary to scleroderma or other disease states	Quality of life and cost effectiveness When compared to liver and kidney transplants, the long-term outcomes of LT are worse. Influence of pre-operative diagnosis Influence of the type of surgical procedure Survival benefit	*FUNCTIONAL OUTCOMES* -Overall quality of life during post-Tx	2057	US
Kidney/Liver	DGF-Acute kidney injury	Survival outcomes will vary based on disease type, age, surgical procedures, etc	Pilot check lists for management of ALF	17,878/7127	US
Pancreas	**What is pancreatic islet transplantation** Pancreas transplants are most often done when a patient also receives a new kidney.	MANAGEMENT Immunosuppressants Immunobiology, diagnosis, and treatment of rejection	PANCREAS TRANSPLANT OUTCOMES post-transplant -Rejection status -Adverse effects Diseases aquired after transplants.	228	US

Stem Cells	Multiple diagnosis	Depends on what procedure was done.	Different patient protocols are designed per study.	N/A for this study	

Quality Management in a clinical research setting

The agency that I worked through was the department of quality management, which oversaw all clinical research trials in the Hanover medical school. My directors team contained ~ 5 people, and the second team had ~20 people working on different projects for the Hanover Medical School in biostatistics. The population they focus on are young pediatric and adult patients that are extremely ill and require an organ transplant immediately. The purpose of having a quality management protocol in place, is to make sure all clinical trials are being done properly and within the standard operating procedures. The overarching health problem that quality management systems deal with are making sure all clinical trials are done within the scope of good clinical practice (GCP), SOP's and within the protocol. Short-term goals are to ensure a safe start to the trial and the risks to the patient are low and not harmful. Long-term goals for a clinical research trial are to approve the end result as a way to improve/save a life.

The objectives of my internship were as follows: to create an academic literature review and research Quality Management and the type of clinical pathways use in organ transplantation. I was apart of several training sessions on quality management, organ transplantation; writing SOP's, and learning how to write/give an internal audit in a clinical research trial going on at the University Hanover medical school. One study I was working on was a new initiative in sharing data with other clinical researchers in the field of organ transplantation. I was asked to provide feedback on the subject and how the US would feel about this particular plan.

Evaluation of Data Sharing Initiative (ICMJE)

Germany, is currently in the works of creating a system where all clinical trials will be required to responsibly share data generated by interventional clinical trials because participants have put themselves at risk. In a growing consensus, many funders around the world- foundations, government agencies, and industry, now mandate data sharing (New England Journal of Medicine, 2016). As a condition of consideration for publications of a clinical trial report in the member journals, the ICMJE proposes to require authors to share with others the de-identified individual-patient data (IPD) underlying results presented in the article (including tables, figures, and appendices or supplementary material, no later than 6 months after publication (New England Journal of Medicine, 2016). Authorizing reliable data sharing is a major endeavor that will shape the fabric o how clinical trials are developed and conducted, and how that data will be interpreted (New England Journal of Medicine, 2016). This requirement will revolutionize clinical studies, which will save time, money and patients from redoing projects that have already be attempted of done successfully. It also aims, in part, to prevent selective publication and selective reporting of research outcomes and to prevent unnecessary duplication of research effort (New England Journal of Medicine, 2016). Data sharing will increase confidence and trust in conclusions drawn from clinical trails.

Initiating a Global Virtual Lab

Another stride being made in clinical research is the design of a global virtual lab within the United States. Currently, the US is working on a **Global virtual lab** for transplantation as a means of developing and disseminating detailed and rigorous protocols for monitoring of alloimmune responses. Global virtual labs are aimed at making standardized testing methods and expertise more accessible to the global transplant research community conducting the clinical trials. This new tool will determine the (+/-) effects that have been undetected with biopsies or standard measurements of donor-specific antibodies. This new tool will allow for communicating on a global scale with researchers/clinicians around the world. Serveral pros/cons and ethical legalities need to be worked out for this to be a functional option. Also, the assessment of outcomes after transplantation is important for several reasons: it provides patients with data so that they can make informed decisions about the benefits of transplantation and the success of the

transplant unit; it informs commissioners that resources are allocated properly; and it provides clinicians reassurance that results are acceptable or, if they are not, provides early warning so that problems can be identified, corrections can be instituted early, and all interested parties can be reassured that scarce resources are used fairly.

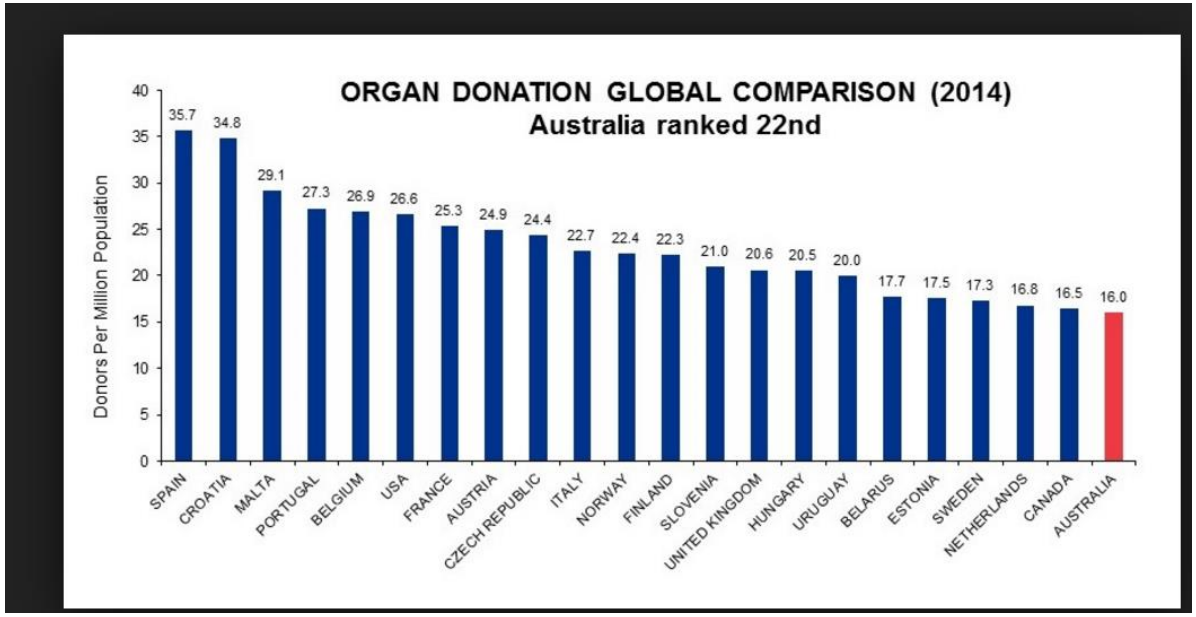
- RISK ADJUSTMENT
- METHODS FOR COMPARING PERFORMANCE
- WITHIN-CENTER MONITORING TECHNIQUES
- BETWEEN-CENTER MONITORING TECHNIQUES
- Cross-Validation Methods
- Success will have a multitude of reasons and certain organs like the liver, kidney and lungs, will have data showing higher trends compared to the heart or pancreas.

Pilot Checklist for Acute Liver Failure: ICU

In Germany, hospitals are taking a new route in providing excellent patient care before, during and post surgery. An acute liver failure checklist was created for the ICU to develop a management strategy to ensure patient safety and efficacy of staff management. The checklist can be utilized among multiple provides in different areas. The Initial checklist was developed from published guidelines and expert opinion. A total of 81 surveys involving management of 116 patients were done during a pilot testing period. The checklist underwent pilot testing at 11 academic liver transplant centers in US and Canada. An anonymous, written survey was given to assess overall usability and feasibility of the checklist.

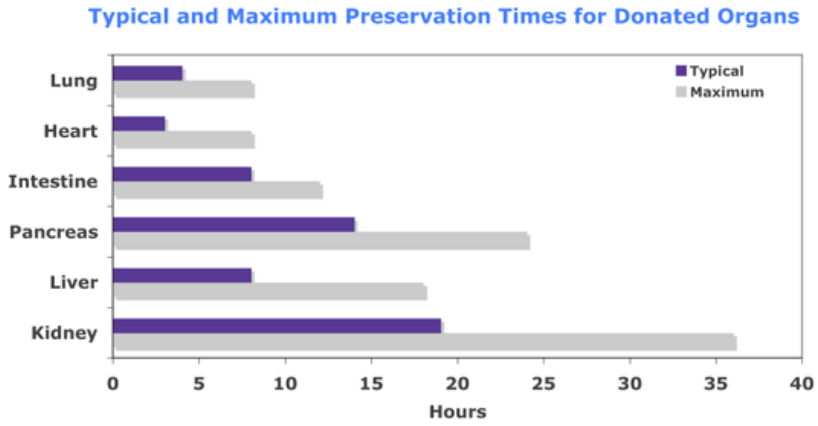
Results/Findings

Although, there is extensive knowledge in the field of organ transplantation, there are still too many gaps that need to be filled. These include death post-transplantation, incidences of infection/diseases and a decrease in long-term survival rates. Shown below is an example of the the country leading the way in organ donation on a global health scale. Spain ranks number one, yet for the US they're ranked 6th. Spain has the highest organ donation rate due to outstanding donor detection and organ procurement and all other countries are lagging significantly behind. Spain has accomplished something the US will aspire to accomplish in the next 5 years.



Although strides have been made, there are still several gaps present. For the people to find information on clinical pathways hospitals use as guidelines, it was nearly impossible to find. Also, there are still too many challenges face in organ transplantation i.e. heart transplantation post-transplant. The discouragement being there is has been no changes in decades and the current shortage of

organs is also an issue. The other gap in the field is the lack of patient education for potential problems post-transplantation. Germany is currently trying to fix this problem with a quality management system guide in organ transplantation. This QMS guide allows doctors to have a set of standards to follow, but after each section in the guide there is a survey of how each doctor viewed its feasibility. Shown below is another advancement made in the field of the total maximum time an organ can be transplanted on ice or machine. This graph is also being update as we speak.



Conclusion and Future Steps

As interest in value-based healthcare continues to drive use of pathways, we need to better understand how they impact patient experience, outcomes and expenditures. Organ transplantation is a growing field and heading in the right direction. Currently, there are over 300 clinical trials going on in Germany, and quality management systems have a huge role in making sure they are done with precision, efficacy and provide the adequate safety to all patients participating. The field of organ transplantation requires more than ever, more research on uncovering new strategies in dealing with the growing disparity of organs, as well as, decreasing the risk factors post-transplantation. Programs will benefit by incorporating focus group interviews for the doctors and patients, and conducting a quantitative data analysis on the primary data. All clinical research trials play an important role in providing life to patients in need. Ten years from now the goal is to create organs that can be self-sufficient, and not having to rely on organ donation. For the purpose of QM in organ transplantation, through observation: A "one size fits all" approach to transition won't work. We must work with each individual patient's unique physical, cognitive and psychosocial abilities. We need to continue collecting & examining global data on the practices, safety, efficacy, quality & epidemiology of allogeneic transplantation, and on ethical issues including living donation, in order to update the WHO Guiding Principles on Human Organ Transplantation (WHO, 2010). The use of international relations is still non-existent within clinical research. Until these relations are better established the field of organ transplantation will not excel.

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Appendices

Application of MPH coursework

Final Learning Objectives

Goal 1:				
Objectives (S)	Activities	Start/End Date	Who is Responsible	Tracking Measures
Quality management & clinical pathways use in organ transplantation centers in U.S and EU.	Literature & research, (), compilation of summary reports and presentation.	May 26, 2016	C. Rodrigues & M. Barthold	Checking in every few hours and going over each step to ensure I was on the right track.

Goal 2:				
Objectives (S)	Activities	Start/End Date	Who is Responsible	Tracking Measures
Standard operating procedures, formatting and (..)	Attended training sessions	June 23, 2016	C. Rodrigues & M. Barthold	

Goal 3:				
Objectives (S)	Activities	Start/End Date	Who is Responsible	Tracking Measures
Working on an Audit for a current clinical trial in progress	Working on a moc audit to understand the format techniques and what goes into an audit	June 27, 2016	C. Rodrigues & M. Barthold	Moc interview

Goal 4:				
Objectives (S)	Activities	Start/End Date	Who is Responsible	Tracking Measures
Evaluation of data sharing Initiative ICMJE	Literature review	May 26th-June 26th.	C. Rodrigues & M. Barthold	Presentation review
sharing Initiative ICMJE	presentation of pros/cons with team.	*		

Master of Public Health Program
MPH PROGRAM COMPETENCY INVENTORY

USF MPH Competencies	Proposed Activities	Number of Hours (Estimated)
1. Assess, monitor, and review the health status of populations and their related determinants of health and illness.	Internalized data sets of organ transplant donors/recipients	5/hr
2. Demonstrate the ability to utilize the proper statistical and epidemiologic tools to assess community needs and program outcomes.	N/A	
3. Identify and prioritize the key dimensions of a public health problem by critically assessing public health literature utilizing both quantitative and qualitative sources.	Created an academic synopsis utilizing 15-20 peer-reviewed literature on clinical pathways in organ transplantation	10 hours
4. Specify approaches for assessing, preventing, and controlling environmental hazards that pose risks to human health and safety.	N/A	
5. Apply theoretical constructs of social change, health behavior and social justice in planning community interventions.	Helped analyze data sets to show the trends of social change	~2-3/hr
6. Articulate the relationship between health care delivery and financing, public health systems, and public policy.	N/A	
7. Apply evidence-based principles to the process of program planning, development, budgeting, management, and evaluation in public health organizations and initiatives.	I learned how the department of QM does their program planning, and evaluations within clinical trials.	2/hrs
8. Demonstrate leadership abilities as collaborators and coordinators of evidence based public health projects.	I collaborated with the director to help uncover new evidence-based practices in quality management	5/hr
9. Identify and apply ethical, moral, and legal principles in all aspects of public health practice.	Uncovered new routes to increasing moral standards with my director	2/hr
10. Develop public health programs and strategies responsive to the diverse cultural values and traditions of the communities being served.	N/A	

11. Effectively communicate public health messages to a variety of audiences from professionals to the general public.		
12. Advance the mission and core values of the University of San Francisco.		
CEPH Core Knowledge Areas	**Proposed Activities**	**Number of Hours (Estimated)**
Biostatistics	Was shown multivariable studies and how it could improve QM in organ transplantation.	2
Epidemiology	Created new avenues in the route of epi and how it could apply new treatment avenues.	3
Social and Behavioral Sciences	Learned all about clinical research and organ transplantation, as well as, how to apply these new skills.	3/hr
Environmental Health	N/A	
Public Health Administration and Leadership	N/A	
Cross-Cutting/Interdisciplinary Values	**Proposed Activities**	**Number of Hours (Estimated)**
Communication and Informatics	Communicated effectively with all colleagues and worked on my presentation skills.	10/hr
Diversity and Culture	N/A	
Leadership	Worked on creating my own synopsis to present to the director and board of directors.	10/hr
Professionalism	Took initiative on my own and proposed my own ideas on how things could be improved.	10-15/hr

Program Planning	N/A	
Public Health Biology	N/A	
Systems Thinking	Learned discipline in pursuing knowledge in a new field (Quality management). I also learned how to search new data base systems.	5-10/hr