MEMORANDUM

TO: Bioethics S13 Class
FROM: Professor Pope
DATE: April 2, 2013
RE: Midterm Exam Feedback

The midterm exam counts for 25% of your overall course grade, 75 of the 300 total course points. The only "real" letter grades are those reported to the Registrar based on the sum of your quizzes, midterm, and final exam. Nevertheless, I have indicated "estimated" midterm letter grades for informational purposes only.

The range of scores was from 41 to 69.
The average score was 54.1.

Attached please find:

1. The score sheet for the midterm exam
2. A model exam answer
3. A chart of numeric scores correlated to exam numbers
4. (I will also post on TWEN a link to an Authorstream video that addresses some common issues that I saw.)

If you want more individualized feedback on your specific exam, please let me know. You, of course, already have a copy of the exam answers that you submitted.

Exam ID _____

Professor Pope, Bioethics
Midterm Exam Scoring Sheet (Spring 2013)

Multiple Choice (1 point each = 30 points)

1. A	**7. C**	**13. C**	**19. B**	**25. B**
2. C	**8. C**	**14. B**	**20. A**	**26. D**
3. D	**9. B**	**15. B**	**21. C**	**27. C**
4. C	**10. C**	**16. A**	**22. A**	**28. A**
5. D	**11. C**	**17. A**	**23. E**	**29. D**
6. D	**12. D**	**18. C**	**24. B**	**30. E**

Short Essay 1 (10 points)

Systematic		
This is experimental and non-validated therapy. But that does not necessarily mean that is constitutes research. It is best described as "clinical innovation" – for treatment.	--	
This intervention is directed to just one individual patient, as a last resort, to benefit that one particular individual. There is no non-clinical study or examination of this patient, much less as compared to other patients.	**5**	
Generalizable		
The purpose or "design" of this intervention is neither to test a hypothesis nor to gather information. No knowledge can be extended from this one case.	**5**	
TOTAL	**10**	

Short Essay 2 (20 points)

Tube for one obese patient		
This would be the same analysis as Short Essay 1. The initial use of the tube is clinical innovation.	**3**	
Adoption as hospital practice		
This makes the use of the tube more systematized. But it is still not for an investigation, to test any hypothesis. On the other hand, the policy might be tentative, depending on the results that will be monitored.	**3**	
It is unclear whether any knowledge is generalizable.	**3**	
Tube at in-service training		
Now the knowledge (that the tube "can" work in such situations) is being generalized.	**3**	
On the other hand, it is generalized only to the staff at this same hospital. It could be fairly characterized as clinical innovation - at the facility level.	**4**	
It is still unclear whether this is systematic investigation.	--	
Alterations, Patent and License		
Now the knowledge is definitely generalized. And it is evaluated to improve the design.	**4**	
For publication or for FDA approval, the research must have been IRB-approved. But the research is already done, and it was not approved. Furthermore, the IRB could be sanctioned for failing to monitor what turned out to be research.	--	
TOTAL	**20**	

Short Essay 3 (15 points)

Research		
While this investigation/study is non-medical, the regulations are not limited to "medical" research. The regulations covers all (1) research that is (2) with human subjects and (3) federally funded.	--	
This research is a systematic investigation to test a hypothesis about payment incentives. It is comparing the effect that withholds versus pure capitation have on physician behavior.	**2**	
The research may not be generalizable, because it will only be used in-house.	**2**	
On the other hand, the regulations require only that the knowledge be "generalizable" not that it actually be "generalized."	**3**	
Human Subjects		
Physicians - The researchers are altering the physicians' environment and collecting data about them.	**2**	
Patients – The researchers are collecting data about them.	**2**	
Federally Funded or FWA		
The regulations do NOT apply to ALL research with human subjects. The research must be federally funded or subject to a FWA.	**2**	
It is unlikely that a private HMO has either.	**2**	
TOTAL	**15**	

Not perfect. But a well written and organized exam answer.

Short Answer 1

Good reading

The federal regulations define research in section 46.102. Research is "systematic investigation" designed to develop and contribute to generalizable knowledge". This gives us a two part test to determine whether a study is research covered by this regulation: 1. Systematic investigation and 2. Designed to develop or contribute to generalizable knowledge.

Good use keys

Systematic Investigation

The oncologist will be doing systematic investigation. Even if the oncologist only gives the ABC drug to this one patient it can still be systematic. Generally cancer patients receive medicine routinely, which I will assume is the case here. This ABC drug will probably be administered more than once and then the patient will be evaluated to see if the patient is improving or having any reaction to the drug. This is testing and evaluation which the regulation gives as an example of systematic investigation. The oncologist is testing the drug because she is administering it to a patient for a cancer that it is typically not used to treat. And it is evaluation because the oncologist will then evaluate the results to see if it is working.

But that is not the facts here

Single Pt

How then can research ever be independent of medicine? Isn't all clinical treatment then automatically research?

Generalizable Knowledge

It is not likely that this going to be used for generalizable knowledge. There is no indication in the facts given that the oncologist intends to use the results for anything other than to improve her own practice and the quality of life for this patient. If the oncologist was publishing the results or helping the researchers by giving them information then it would be used for generalizable knowledge. There is an argument that this may be used for more than quality improvement. ABC drug is being tested for use on colon cancer and the oncologist has been talking to the researcher. However, without more information it appears that this is not the case. Based on the facts presented I believe that the oncologist will not be using the information for anything other than quality improvement.

Although the oncologist is doing systematic investigation of the ABC drug this is not research because the information obtained will not be used for generalizable knowledge.

Short Answer 2

As I stated in the last question, research by definition has two parts: 1. Systematic investigation and 2. Designed to contribute or develop generalizable knowledge. I also stated in the previous

question that if the knowledge obtained is only used for quality improvement within one's own practice then it is not considered generalizable knowledge.

Again good to structure & organize the analysis using the relevant applicable legal test elements

Systematic Investigation

It is difficult to say that this will be considered systematic investigation. There is no indication that this happened more than once before it was adopted as regular practice. The nurse made a suggestion in an urgent situation and it worked out well. Because of this one incident the hospital decided to implement the use of the "pediatric tube" as regular practice. Systematic means methodical or routine, which would mean more than once. And investigation is a formal inquiry which this was not; it was a nurse thinking quickly in an urgent situation. This fails to be research based on this and assuming that no further investigation was done each of the subsequent variations of the problem would also fail. But for the rest of the problem I will assume that this was adequate systematic investigation.

Generalizable Knowledge: Regular Hospital Practice

This practice was probably not done to contribute generalizable knowledge in the original situation. A nurse in the hospital suggested the use of the "pediatric tube" because she saw a problem. She originally made the suggestion because she was in an urgent situation and she had previous experience in a children's hospital. The hospital then decided to test this method and because it worked they began using it as a regular practice. There is no indication that anything further was planned. The hospital had a problem within the hospital and they came up with a solution. Improving the quality of practice within the hospital is not research.

Generalizable Knowledge: In-service Training

When the nurse presents the "pediatric tube" approach at the "in-service training" may be a contribution to generalizable knowledge. However, this may only be considered a use for generalizable knowledge if the nurse is training nurses from other hospitals. If the training is for new nurses, or continuing education for nurses employed at the same hospital then it probably will not be considered research for the same reasons as I noted above. Quality improvement of one's own practice is not use for generalizable knowledge.

Generalizable Knowledge: Patent and Licensing

Finally, if the nurse makes alterations to the "pediatric tube" and seeks a patent and license then this is more likely to be considered part of her research. The fact that this will now be used for generalizable knowledge makes this more likely to be research. Some may argue that this is not generalizable knowledge because it is not necessarily being published. But the fact that a product will be created and widely used is the same thing. Products that go on the market must be researched. However, one could argue further that the development of the product is in hind

sight. The definition of research by the regulations says that the systematic investigation must be designed to contribute to generalizable knowledge. If the investigation that the nurse and hospital did initially was only intended to be used for quality improvement of the hospital then this may not be considered research. I believe that based on the way the statute is written this may not be research still. In this case the systematic investigation was not designed to contribute to generalizable knowledge.

Short Answer 3

Is it research?

The first step in determining whether or not the rules apply is determining if it is actually research. In order to be research, the activity taking place must be a systematic investigation designed to contribute generalizable knowledge. YooCare ha definitely developed a systematic investigation in order to find out the information they are seeking. YooCare's study on the capital status versus the withhold status methods of payment is a systematic investigation. But the facts clearly state that YooCare intends to keep the results for their use alone. There is an argument that can be made that this study should still be considered as designed to develop generalizable knowledge because of the amount of people that this will affect. YooCare is a private HMO and although only 25 PCPs are involved in the study they probably have many more PCPs working for them.

Is it Human Subjects Research?

The Common Rule tells us that a human subject is a living individual about whom an investigator obtains data through interaction or obtains identifiable private information. Although there are living individuals involved in this study I do not think this would qualify as human subjects research. The investigators are not interacting or intervening with the patients. The PCPs are interacting with the patients but this is not the subject of the research. The method of payment to the PCPs is the subject of the study. There is a possibility that the investigators are obtaining private identifiable information about the patients though. If the investigator obtains the name or the patient file then this is human subjects.

Funding?

The final question relevant to this project is does YooCare receive any federal funding. The regulations only applies to those studies and researchers that receive federal funding. The facts

indicate that YooCare is a private HMO and if this means that it does not receive any federal funds then the rule does not apply.

Conclusion

The Common Rule probably does not apply to this study conducted by YooCare. YooCare is a private company and it doesn't appear that they receive any federal funding. It is also possible that the study is completed without collecting any information on the patients and therefore would not be human subjects research. Finally, this may not even be research.

EXAM ID	MC 30	E1 10	E2 20	E3 15	TOTAL 75	EST GRADE
0316	19	9	14	5	47	B
0619	22	8	14	8	52	B
0829	28	10	9	10	57	B+
1090	25	5	16	9	55	B+
1354	18	6	11	7	41	B-
2563	22	6	13	5	46	B
2737	23	4	15	0	42	B-
3037	22	8	16	10	56	B+
3655	19	10	19	11	59	A-
3658	20	6	13	10	49	B
4444	24	10	16	13	63	A-
4615	22	7	8	13	50	A-
4681	22	8	11	2	43	B-
4819	25	8	15	11	59	A-
5164	22	8	16	11	57	B+
6223	25	10	15	13	63	A-
6799	22	7	11	9	49	B
7591	25	10	16	10	61	A-
8059	21	8	15	6	50	B
8185	23	9	20	13	65	A
9046	22	10	14	6	52	B

Some students asked for further explanation of some of the multiple choice questions. I have reprinted below: (a) the question, (b) the student's query, and (c) my response.

2. Greg is working on his dissertation. Greg plans to interview principals in neighboring high schools. Greg plans to collect data about the personal experiences that the principals have had with disruptive students and what types of disciplinary actions they took. Identifiers will be collected. This study would be categorized as:

A. Expedited Review
B. Exempt Review
C. Full Board Review
D. Not Human Subjects

STUDENT: (B) This study would be categorized as exempt review under § 46.101(b)(1) because there is involvement of "research conducted in commonly accepted educational settings, involving normal education practices, such as research on the effectiveness of classroom management methods.

POPE: (C) I agree that is (b)(1) applied, then this research would be exempt. But it seems strained to conclude that (b)(1) applies here. The subsection is focused on "normal educational practices" such as "instructional strategies," "instructional techniques," "curricula." In other words, the exception is focused on pedagogy and teaching. Perhaps you thought discipline could fall under "classroom management." I think that is problematic for two reasons. First, that gives it a meaning broader than the other listed examples of instructional strategies. Second, the research subjects are principals, not teachers. The research is about discipline imposed once the student left the classroom and got "sent to the principal's office."

4. Which type of IRB review does not require an IRB "approval" but still requires a determination by the IRB or a designee of the IRB?

A. Full Board Review
B. Expedited Review
C. Exempt
D. All of the above
E. None of the above

STUDENT: (B) § 46.110(b) recognizes that expedited review can be used to review **either** or both of (1) some of all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk, (2) minor changes in previously approved research during the period (of one year or less) for which approval is authorized. If only section (1) is evaluated, then IRB approval is not required.

POPE: (C) Yes, but under that section, the result of the expedited review is either approved or referred for full committee review. Research eligible for expedited review must still be "approved." The word is used six times in this section. In contrast, "exempt" research does not require approval.

5. Christy plans to track the restrictions that U.S. immigration laws imposed on certain ethnic groups. She plans to do this by reviewing passenger lists from ships that transported immigrants to America between 1840 and 1860. This study would be categorized as:

A. Expedited Review
B. Exempt Review
C. Full Board Review
D. Not Human Subjects Research

STUDENT: (A) I ruled out answer choice (D) because I considered the scenario to involve human subject research. Human subject research is defined as data through intervention or interaction with the individuals, or identifiable private information. Christy reviewing passenger lists from ships that transported immigrants to America is considered reviewing identifiable private information. Having a passenger's ethnic origin listed next to their name is exposing private information.

POPE: (D) Yes, the information may be identifiable. But 46.102(f) limits the definition of "human subject" to only LIVING individuals "about whom an investigator obtains "identifiable private information." Nineteenth century immigrants are surely no longer living.

Alice is planning federally funded research study involving children who are 7 to 11 years old. Alice's research involves collecting two urine samples from healthy children to measure amounts of protein. Alice's IRB has determined that assent of children age 9 and older is required for the study. One 11-year-old refuses assent to participate in the study described above.

8. Which of the following procedures best describes the required action?

A. Consent one of the child's parents instead
B. Request the child to reconsider assenting to the study
C. Honor the child's decision
D. Consent both of the child's parents instead

STUDENT: (A) On Quiz #3 on question #4, we were presented with a similar question. On the Quiz we learned that in this type of a scenario, there is no more than minimal risk to the child. Based on this determination, we can look to § 46.404 which requires adequate provisions being made to solicit the assent of the children and permission of their parents or guardians when the

research does not involve greater than minimal risk. However, the child's assent may be waived by the language set forth in § 46.408, which states that if the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, the assent of the children is not a necessary condition for proceeding. The children in this scenario are seven to eleven years old. Especially at the age of seven, children are not capable of reasonably being consulted on whether to undergo the research or not. Therefore, the children's' consent should be waived.

POPE: (C) Yes, 46.408(a) does say that "If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted . . . the assent of the children is not a necessary condition for proceeding with the research." But the question itself specifies that the researchers concluded "that assent of children age 9 and older is required for the study." 46.408(a) further provides that "when in the judgment of the IRB the children are capable of providing assent" then the IRB "shall determine that adequate provisions are made for soliciting the assent." Since this IRB determined the children are capable, it should honor the refusal.

13. The death of Ellen Roche exposed the following problems with research at Johns Hopkins?

A. There were not sufficient IRB resources relative to the number of research protocols
B. Failure to respond adequately to a previous adverse event
C. Both A and B
D. Neither A nor B

13. (D) On page 1 of "Protecting Research Subjects – The Crisis at Johns Hopkins" by Steinbrook, the problems with the research were identified, and did not fall under answer choices (A) or (B). "The shutdown at Johns Hopkins has focused attention on the safety of medical research, particularly when the subjects are healthy volunteers or are employed at the institution where the research takes place. The shutdown has also spurred efforts to improve the effectiveness of the various groups that have a role in protecting research subjects, including investigators, institutional review boards (IRB's), sponsors, and the institutions where the research is conducted." Therefore, neither answer choice (A) or (B) are exactly correct.

POPE: (C) The concluding paragraphs of the NEJM article recap the problems. For example, "until June 2001 there had been only one IRB committee . . . responsible for the review of 800 new proposals and the annual reviews resulting from them. We view this as grossly inadequate." Earlier in the article, the researcher "was criticized for not reporting the symptoms in the first subject [subject 1] promptly."

17. Milo is a developmental psychologist. He proposes videotaping interactions between pre-school children and their caregivers in a laboratory setting to determine what methods of communication most effectively manage aggression.

A. This is human subject research
B. This is NOT human subject research

STUDENT: (B) Human subject research is defined as data through (a) intervention or interaction with the individuals, or (b) identifiable private information. If Milo is videotaping pre-school children and their caregivers in a laboratory setting, there is no intervention or interaction between Milo and the children or caregivers. Also, Milo does not need to obtain the children or caregivers' identifiable private information in order to videotape them in a laboratory setting.

POPE: (A) Audiotapes and videotapes are considered identifiable information, even if no names are included. The faces and behavior of the subjects are recorded.

21. The Nuremberg Code:

A. Had an immediate and profound influence on how research was conducted in the United States
B. Resulted in the establishment of the OHRP
C. Was not considered relevant to research practices in the United States

STUDENT: (A) I did not choose answer (C) because the Nuremberg Code is considered relevant to research practices in the United States, as issues of human subject research are the root of many law suits today. The Nuremberg Code did have a profound influence on how research was being conducted in the United States today; however, I do not believe the Code had an "immediate" influence. I was caught between answer choices (A) and (C). Since, answer choice (C) was "more wrong," I chose answer (A). Part of my confusion with this problem was the time frame. The answer choices were stated in the past tense, yet I did not know whether we were required to focus on the distant past or more recent past.

POPE: (C) The Beecher article and other materials demonstrate that A is definitively false. U.S. research ethics remained deficient for decades after Nuremberg. Therefore, even if the timeframe in C is ambiguous, it must be the best answer. It is only ***potentially*** false, in contrast, to A which is certainly false.

26. An investigator is recording non-identifiable information from state records to study the frequency of "handedness" (left hand versus right hand) in a given population. What level of review is most appropriate?

A. Expedited review by a designated IRB member
B. None
C. Review by a convened quorum of the IRB
D. Determination of exemption

STUDENT: (B) Studying left versus right handedness does not fall under any of the categories requiring exempt review under § 46.101(b). The research does not even fall under human subject research because there will be no intervention or interaction with the individuals, nor identifiable private information obtained.

POPE: (D) Exemption can be determined under 46.101(a) ***as well as*** under 46.101(b). Under 46.101(a) this investigation would be exempt because it is not "research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency." If an investigation were not exempt under 46.101(a), then one would proceed to analyze whether it might be exempt under 46.101(b).