Human Subject and IRB Issues for Consideration

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The speaker has no conflict of interest to disclose.

Overview

- When is it human subjects research?
- Ethical Issues in Population-Based Genetic Research
- IRB Determinations: Waivers of IC
- HIPPA Research Issues
- Using Research Design to Minimize Risk

When is it Human Subjects Research?

- When it meets the definitions:
  - "Human subjects"
  - "Research"

Human Subjects

Living individual(s) about whom an investigator (whether professional or student) conducting research obtains:

(1) data through intervention or interaction with the individual, or

(2) identifiable private information.

45CFR46.102(f)

Human Subjects

- **Intervention**: Includes both physical procedures and manipulation of the subject or his environment for research purposes.
- **Interaction**: Includes communication or interpersonal contact between investigator and subjects

45CFR46.102(f)

Human Subjects

Private Information: Includes information about behavior that occurs in a context in which an individual can **reasonably expect** that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can **reasonably expect** will not be made public (e.g. med record, school).

45CFR46.102(f)

Human Subjects

Private information **must be individually identifiable** (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

45CFR46.102(f)

Research

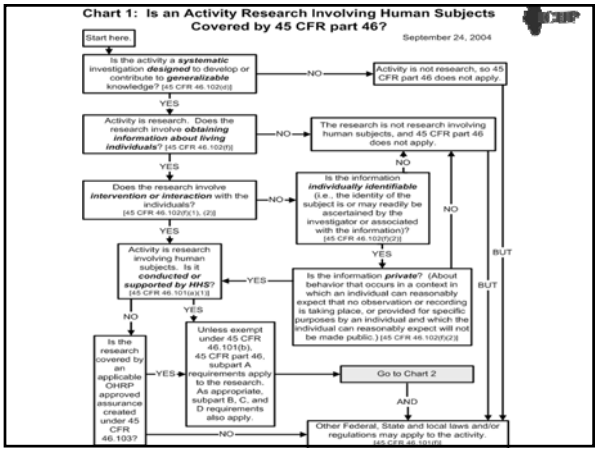
- *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and **service programs may include research activities**.

Belmont Distinction: Clinical Practice versus Research

- "Practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.

Belmont Distinction: Clinical Practice versus Research

- "Research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.



Public Health Research vs. Non-Research

- Not so easy to distinguish
- Public Health Research versus Non-Research
  - Neither is focused on the interests of the individual
  - Interventions and activities are always assumed to be generalizable

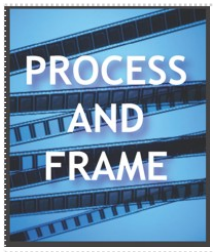
Danziger
09-038

Questions:

1. Which of the following are the three principles basic to the protection of human subjects?

    a. Respect for persons, Beneficence, Justice
    b. HIPAA, Respect for persons, Beneficence
    c. Privacy and confidentiality, Beneficence, Justice
    d. 45 CFR 46, Belmont Report, ICH

2. Which of the following regulations govern human subjects research?
    a. 45 CF R46
    b. Health Insurance Portability and Accountability Act (HIPAA) (45CFR160-164)
    c. 21 CRF 50 & 56
    d. All of the above



ICHP Annual Meeting September 11, 2009

Basic Research and Statistics Roundtables: How to Start Your First Study
How to Select a Research Topic. Michael Fotis

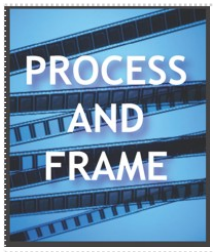
A good way to prepare your first study is to conduct a comparison of current practice at your workplace to a consensus standard. The ASHP 2015 initiative is an example of a good starting point. USP 797, TJC, almost any recognized therapeutic or practice guideline are other options. Wait until your second study to cure chronic diseases, and leave something for the rest of us to do!

These roundtable discussion questions are addressed in Great Research Questions: Lipowski, Am J Health-Syst Pharm—Vol 65 Sep 1, 2008.

- Give an example of an aspect of practice that is unwieldy and problematic, of resources in short supply, or of outcomes that are disconcerting.
- Give an example of work arounds and quick fixes.
- Pet theories, and sacred cows.
- Give an example using the ask why 5 times technique
- Compare a dependent to an independent variable
- Give a simple example of a measurement option
- Explain the importance of Effect Size

Good Use of Study Objectives is discussed in Getting Ready for Great Lakes: Fotis, KeePosted April 2009.

- Start out by listing your study objectives. Hopefully they are MUM objectives (Meaningful, Unambiguous, and Measurable).
- Identify a study idea whose findings are interesting no matter what the results.
- Plan to present your results for each of your study objectives and include the name of your objective in the Header for each Results Slide. Include at least one take away point for each of your results slides and insert this statement in an open section of your figure or table. Discussing your results findings by objective helps your audience keep track and also prevents the results slide from getting too busy.
- If your objectives are unclear or even absent than you probably will end up with a mass of raw data to present. Do not present raw data anywhere. You must categorize your data so you and the audience can grasp the significance of your findings. Set your study objectives so that it is easy to categorize your data. Your statistical analysis and your conclusion should also be based on your study objectives.



Other Suggestions:

- Drug Dosing in Pregnancy
- Exposure of CI medications in female patients < 40 not taking contraceptives (this will be a huge topic soon)
- Follow up use study on any FDA report of warnings and advisories- particularly contraindications and black box warnings or off label use.
- Any practice or protocol that is not supported by evidence. This is a good way to develop an outstanding research hypothesis.
- Help out on a project sponsored by one of the ICHP Divisions such as Educational Affairs

Study Task List

1. What is the research question – extensive literature search, do a 1-page write up of main idea
2. Define Target Population
3. Define your study hypothesis in one sentence
4. Develop study objectives from your hypothesis. Goal – only one primary objective, no more than three secondary objectives
5. Select measurable endpoints
6. Define inclusion and exclusion criteria
7. Determine Study Design
8. Calculate sample size and power
9. Prepare research and analysis plan
10. Finalize protocol
11. Develop case report form and informed consent form
12. Develop data dictionary
13. Recruit/Contact appropriate support personnel, co-investigators, etc.
14. Review your protocol and other study forms with co-investigators
15. Submit for IRB/ERB review
16. Upon final approval by IRB/ERB START YOUR STUDY!!!

Centers for Medicare & Medicaid Services (Adapted)

Study Protocol Format

Adapted 2009

TITLE PAGE: Title of study, contact information, sponsor information (if applicable)

TABLE OF CONTENTS

EXECUTIVE SUMMARY

The Executive Summary is a one page summary that includes a highly condensed version of the study objectives, background, importance, and design (including requested data files). This summary will be the cover page of the research protocol and should be detailed enough to allow any CMS representative reviewing the executive summary to understand the study being proposed. Although the Executive Summary should be submitted as the cover page, it may be beneficial to complete the summary after finishing the final protocol.

Additionally, the Executive Summary should *briefly* address each of the following:

1. How the study has the potential to improve the quality of life for Medicare beneficiaries or Medicaid recipients, or improve the administration of the CMS programs.
2. The measures to be taken to ensure that the use of these data involves no more than minimal risk to individuals. A more comprehensive overview may be presented in the Database Management section of the protocol.
3. Could the research be conducted without individual level authorization? Explain.
4. Could the research be conducted without access to these individually identifiable data? Explain.

INTRODUCTION

Title:
The researcher should be succinct in titling their project. Use keywords, phrases, or descriptors that will highlight the population of interest, the medical problems of concern, and the health policy issues of importance.

Objectives:
The objectives should pinpoint what the researcher plans to do and expects to achieve. The number of objectives should be relatively few and listed in approximate order of priority or importance. The objectives listed should underscore the major elements of work that are realistically achievable.

Background:
The background should succinctly highlight gaps in the current knowledge or practice in the field of study. The researcher must show that he or she understands the important studies that form the foundation for the protocol and indicate how the project will go beyond them. Please include a literature review. The literature review need not be lengthy, but it should be reasonably comprehensive and up-to-date.

The researcher is not expected to review all the relevant literature in great detail; if he or she is conversant with other bibliographies or literature reviews, they should be cited. If there is no literature or body of knowledge in the area proposed for study, this should be stated.

Centers for Medicare & Medicaid Services
Study Protocol Format

Importance:
There are two main points that should be addressed here: the significance of the question or study issue proposed and the significance of the researcher's particular project. This is the place to make a strong case for the importance of the project being proposed. For example, the proposed study may add to the general body of knowledge, expand the possible ways to organize and deliver health services to meet a particular human need, or it may do both. The point is to deliver a credible, straightforward argument for the contributions that the work will make.

RESEARCH QUESTIONS AND METHODS

Hypotheses/Study Issues:
If there are hypotheses to test, they should be stated explicitly. If there are no specific hypotheses, the application should discuss the issues that prompted the researcher to undertake the project.

Study Design:
The basic objective is to describe how the project will operate. In some studies, Medicare or Medicaid data will be used to supplement other data. In this instance, the researcher should briefly state the design of the overall project and then describe in detail how the CMS data being requested will be used in the study. Uppermost in the reviewers' minds are the questions of how each piece of information relates to the hypotheses to be tested, issues to be studied, or program(s) to be demonstrated. It is a good idea to consult an epidemiologist, statistician, econometrician, or some other person well acquainted with basic research methodology when planning the design and analysis of the project. The study design must present a solid chain of reasoning. The study design, at a minimum, should:

- Describe the sample population to be studied and the method to be used to select or identify the study population in the data files;
- Discuss the issue of precision or power of the study and the strength of its eventual conclusions. If applicable, indicate whatever power calculations might have been done to justify the sample size and comment whether the sample size will permit accurate generalization to larger populations;
- Give a specific description of the match between what is to be investigated and the data files and variables to be used in the analysis;
- Briefly state the dependant (or response) variables, the independent (treatment or explanatory) variables, and the factors that may need to be measured or accounted for because they might otherwise confound the analyses;
- If relevant, discuss the project's cross-sectional aspects (comparisons in one time period) and longitudinal aspects (comparisons over time).

Data Limitations:
It is important to note potential limitations of the data in relation to the proposed study and to identify the efforts that will be made to address those issues. For example, noting that the data does not contain information regarding services not covered by, or billed to, Medicare and how that might affect the results. It is better to show that consideration has been given to what the potential limitations are rather than have reviewers assume that the researcher was not aware any existed.

Database Management:
The protocol should explicitly address how the data files will be held, managed, and processed. For example, who will have the main responsibility for organizing, storing, and archiving the data? Who will maintain computer data tapes and make needed work files available to those who will analyze the data? How will the privacy of information of beneficiaries in the files be guarded and guaranteed? Include any measures that discuss how patient confidentiality will be maintained in accordance with HIPAA.

EVALUATION AND ANALYSIS PLAN

Analysis Plan:
In this section, the application should explain, as clearly as possible, how the data would be analyzed. This section should convince reviewers that the proposed methods are consistent with the hypotheses/issues to be studied and the data to be collected, and it should persuade them that the data will support the level of analysis planned.

Analytic Methods:
This section should discuss specifically what analytic methods are expected to be used to address which questions. It is often helpful to give examples of the analyses or to show what the tables of results might look like. Often, discussing hypothetical findings based on likely values of the data which will eventually be collected is a useful device for making the analysis plan seem less abstract. The goal is to try to aid reviewers in visualizing the data set that will be compiled, so that they can think along with the researcher about what methods of analyses seem appropriate and reasonable to address the hypotheses/issues to be studied.

WORK PLAN

Description of Tasks:
The proposed work should be sufficiently well planned that the researcher can specify a set of tasks that will cover all the activities needed to complete the project. The aim is to identify all the tasks to be accomplished regarding study design and analysis. In addition, note that one task will probably involve producing a final report. Every task noted here should have some corresponding description in the study design and/or analysis plan section(s) to show how it will be accomplished; every major activity targeted for completion should have a corresponding task.

Time Schedule:
The application should provide a Gantt chart or some other diagram to illustrate when the tasks outlined above will be completed, in what order, and how long they are expected to take. This is commonly done in terms of elapsed months (e.g., for a 2-year study, months 0 through 24 would be one axis of your chart). It is helpful to adopt some conventional symbols, such as an asterisk or triangle, to show when specific milestones are to be achieved.

Level of Effort of Personnel:
This section is commonly shown as a table, in which the researcher lists the key individuals (by name or by task) and the number of days they will devote to each task.

For multi-year projects, the researcher should show total days in each year. Total days per year should be equivalent to whatever percentage of time is shown for these individuals in the budget

document. Note that reviewers pay attention to these figures. Too little time for key personnel suggests that the researcher may have an unrealistically optimistic view of what can be accomplished.

Centers for Medicare & Medicaid Services
Study Protocol Format

QUALIFICATIONS OF KEY STAFF

To the extent possible, persons the researcher believes are crucial to a successful project should be named in this section. Even very good projects will look dubious to reviewers if the principal investigator or critical staff are "to be named." The qualifications of key personnel named in this section should be discussed. A paragraph or two per person describing their background and experience most pertinent to this project will suffice. This or a parallel section could also be used to describe any experience the researcher's organization has had in conducting similar projects, especially insofar as that experience will be available as backup and support for the key staff. If the researcher has special data collection or analytic needs, this is the place to indicate that the researcher has the right personnel for the job. Often, these individuals can be consultants rather than project staff. For instance, the project may require a physician for certain tasks and a statistician or economist for other tasks. To the degree possible, the application should indicate who these people are or say what types of individuals will be recruited later.

IMPLEMENTATION POTENTIAL

This is not a long section, typically, but it is an important one. It is where the researcher discusses the expected use, generalizability, applicability, and dissemination of the work.

References

Cite all relevant literature in proper format.

Appendices **- these can be many and varied**

Possibilities:

Detailed Analysis Plans (tables, report shells, etc.)

Case Report Form

Informed Consent Form

Data Dictionary

Others??

HIPAA Protected Health Information

The Privacy Rule allows a covered entity to de-identify data by removing all 18 elements that could be used to identify the individual or the individual's relatives, employers, or household members; these elements are enumerated in the Privacy Rule. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify the individual who is the subject of the information. Under this method, the identifiers that must be removed are the following:

1. Names.
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
   a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
   b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4. Telephone numbers.
5. Facsimile numbers.
6. Electronic mail addresses.
7. Social security numbers.
8. Medical record numbers.
9. Health plan beneficiary numbers.
10. Account numbers.
11. Certificate/license numbers.
12. Vehicle identifiers and serial numbers, including license plate numbers.
13. Device identifiers and serial numbers.
14. Web universal resource locators (URLs).
15. Internet protocol (IP) address numbers.
16. Biometric identifiers, including fingerprints and voiceprints.
17. Full-face photographic images and any comparable images.
18. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

Post-test questions – Carla Frye

"How to Start Your First Study"

1. One of the requirements of an ASHP-accredited pharmacy residency is to do a research project. What should be your SECOND priority (the first is to develop a research question) in developing your study?
    a. Define your target study population
    b. Prepare a research and analysis plan
    c. Determine your sample size
    d. Write your informed consent

2. True or False
   Clinical trials should have sufficient statistical power to detect differences between groups considered to be of clinical interest. Therefore, calculation of sample size with provision for adequate levels of significance and power is an essential part of planning.

Post Test Questions (PHerout)

1. True or False Randomized controlled trial designs should always be the preferred method to answer any research question.

2. Which of the following is false regarding cross-sectional studies?

a. They are primarily descriptive

b. Can be used for evaluating exposures that do not change over time

c. Can assess causality

d. Are useful for assessing the prevalence of a condition

Use of Statistical Analysis in Clinical Research – Logistic Regression

Kumar Mukherjee Ph.D.
Chicago State University

The speaker has no conflict to disclose.

Objectives

- To select an appropriate statistical test to answer a clinical research question.
- To analyze whether a selected statistical test is appropriate in context of a clinical research question
- To interpret the findings of a statistical test

We will consider Logistic regression as a statistical technique here

Level of Measurement of Variables

- Dependent or Outcome Variable: Only Categorical (two or more than two categories)
  - Example: An adverse event took place (Yes/No). Pain Level (Less, Moderate, Severe)
- Independent or predictor variable: Numeric or Categorical

When to Use logistic regression?

- When the dependent variable is categorical in nature (two or more categories) and the number of independent variables (numeric or categorical or both) are more than one.
- Note that if the dependent variable has only two categories and the independent variable has only two categories one can just calculate odds ratio without using logistic regression

Use of Logistic regression

- It can predict the probability of occurrence of an event for an individual given the characteristics (predictor variables)
- It also helps to compare the probability of occurrence of an event between two or more treatment
- However it predicts in terms of “Logarithm of Odds” of an event taking place

Is Logistic Regression Appropriate in NICE-SUGAR trial?

- Yes. As the primary outcome measure was "Death" – a binary variable (Yes/No)
  The dependent variable is categorical in nature .

Logistic Regression Equation

- In the logistic regression equation the dependent variable is
  "logarithm of odds" of an Outcome Y.
- The logistic regression equation :

$$\log \left[\frac{P(Y=1)}{1 - P(Y=1)} \right] = \alpha + \beta X$$

- Log (odds of p(y=1)) is called Logit (P(y=1))

What to look for in an article using Logistic Regression?

- Significance of overall model (This explains whether all independent variables together can significantly predict the odds of an event taking place)
- Significance of individual regression coefficient (Magnitude, 95% CI or statistical significance of the regression coefficient)

Interpreting findings of a logistic regression

- Please refer to the handout

Study Question 1

- Please refer the article based on NICE-SUGAR trial published in the NEJM. Refer Table 3 (page #1292). Compare the number of death at day 90 vs. number of death at day 28 between Intensive Glucose control group and Conventional glucose control group.

Study Question 2

- Consider the article comparing the effect of early vs. deferred antiretroviral therapy for HIV on survival (Kitahata et.al.) Please look at table 3. How would you compare the effect of Baseline CD4+ count and Baseline HIV RNA level on the risk of death for the group with 351 to 500 CD4+ count?

Thank You!!
Questions?

OUTPUT EXPLANATION FOR LOGISTIC REGRESSION

Scenario: A researcher is interested to know how the GRE score, undergraduate GPA, and area of schooling of students influences the probability of a student getting admission in a Graduate program in Epidemiology in private schools. **The GRE score and Undergraduate GPA are numeric variables, while the "Area of Schooling" is considered as a binary variable (urban/rural)**. Data collected over 400 students were analyzed. The following tables represent output for this analysis.

Variable	N	Mean	Std Dev	Minimum	Maximum
GRE	400	587.700	115.52	220.00	800.00
GPA	400	3.39	0.38	2.26	4.00

This table explains the descriptive statistics (mean, standard deviation, minimum and maximum) about the numeric variables.

Area of Schooling	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	335	83.75	335	83.75
1	65	16.25	400	100.00

This table explains the categorical variable (area of schooling). Here "0" represents "Urban" and "1" represents "Rural". So there are 335 students from urban area and 65 students from Rural area in the sample.

The response variable or the output variable is **binary** in nature here. There can be only two possible outcomes: a) A student is Admitted, b) A student is not admitted. Out of 400 students, 127 are admitted and 273 students are rejected.

Response Profile

Ordered Value	**ADMIT**	Total Frequency
1	1	127
2	0	273

Probability modeled is **ADMIT=1**.

Here we are modeling **admit** being 1 (this means a student is admitted). Note that we could also model **admit** being 0 and our results would be completely reversed in that case, though **the basic findings would remain unchanged**.

Q1. What is the prediction or regression equation in this example?

Answer:
Logit [Prob (ADMIT = 1)] = $\alpha + \beta_1(GRE) + \beta_2(GPA) + \beta_3(AREA)$

This can also be written as:
Log [(probability of ADMIT) / (probability of NON-ADMIT)] = $\alpha + \beta_1(GRE) + \beta_2(GPA) + \beta_3(AREA)$

Model Fit Statistics

Criterion	Intercept Only	Intercept and Covariates
AIC	501.977	486.130
SC	505.968	502.095
-2 Log L	**499.977**	**478.130**

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	**21.847**	**3**	**<.0001**
Score	21.5235	3	<.0001
Wald	20.4017	3	0.0001

This output tests the overall fit of the model. We are just concentrating here on the **Likelihood-ratio test statistic**. Under the model fit statistics, we compare the two models:

Model 1: Logit [Prob (ADMIT = 1)] = α (This is the INTERCEPT ONLY model)

Model 2: Logit [Prob (ADMIT = 1)] = $\alpha + \beta_1(GRE) + \beta_2(GPA) + \beta_3(AREA)$ (This is the complete model)

We obtain here that the maximized value of likelihood ratio ($-2 \log L_0$) for the Intercept only model is equal to 499.977, while the maximized value of Likelihood ratio ($-2 \log L_1$) for the complete model is 478.13

So, the **Likelihood ratio test statistic** is equal to: $[(-2 \log L_0) - (-2 \log L_1)]$

$$= \mathbf{(499.977 - 478.13) = 21.847}$$

Note that this value of 21.847 is reported as the Likelihood ratio test statistic under the section "**Testing Global Null Hypothesis: BETA=0".**

Q2. How do we claim here that our model fits well compared to the intercept only (or the simple) model?

Answer: Under the section Testing Global Null Hypothesis: BETA=0, we have the Likelihood ratio test statistic equal to 21.847. Since our model has three independent variables (GRE, GPA and Area of Schooling) we have the degree of freedom equal to 3. We know that Likelihood ratio test statistic follows a CHI-SQUARE distribution with the degree of freedom equals to number of independent variables in model. Corresponding to alpha (probability of type 1 error) equals to 0.05 and degree of freedom equals to 3, we obtain the critical chi-square value equals to 7.81. Since our obtained chi-square (21.847) > 7.81, so we will be able to reject the null hypothesis that Beta = 0 for the overall model.
You can also check the Pr>chi-sq value (< 0.0001), which is much less than 0.05 to reach the same conclusion of rejecting the null hypothesis.
This means that GRE, GPA and Area of Schooling together can statistically significantly predict (or explain) the probability of someone getting admission in a Graduate program in Epidemiology in private schools.

Now we are going to explore how the individual variables influenced the odds of admission for a candidate?

The LOGISTIC Procedure

Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate (β)	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	-4.6008	1.0964	17.6095	<.0001
GRE	1	0.0025	0.00107	5.3560	0.0207
GPA	1	0.6676	0.3253	4.2123	0.0401
AREA	1	-0.4372	0.2919	2.2443	0.1341

Question: Write down the complete logistic regression from the above output

Answer:
Logit [Prob (ADMIT = 1)] = –4.6008 + 0.0025 (GRE) + 0.6676 (GPA) – 0.4372 (AREA)

Now, we are going to explore the statistical significance of individual coefficients in the logistic regression model.

Question: How do you interpret the effect of GRE on the odds of getting admission?

Answer: Controlling for GPA and AREA of Schooling, for every unit increase in the GRE score, the odds of getting admission increases by Exp (0.0025) = 1.0025 times, or the odds of getting admission multiply by 1.0025.

The Wald chi-square statistic [= (estimate / standard error)^2] shows that p = 0.0207 which is much less than p = 0.05. So at an alpha level of 0.05, we can reject the null hypothesis. The effect of GRE on odds of getting admission is statistically significant

Question: How do you interpret the effect of 10 units increase in GRE score on the odds of getting admission?

Answer: Controlling for GPA and AREA of Schooling, a 10 units increase in GRE score, the odds of getting admission increases by **EXP(0.0025*10) = Exp (0.025) = 1.025** times, or by 2.5% or the odds of getting admission multiplied by 1.025.

Question: How do you interpret the effect of GPA on the odds of getting admission?

Answer: Controlling for GRE and AREA of Schooling, for every unit increase in the GPA score, the odds of getting admission increases by Exp (0.6676) = 1.9495 times, or the odds of getting admission multiply by 1.9495. This effect of GPA on odds of getting admission is statistically significant and we can reject the Null hypothesis H_0: $\beta_{(GPA)} = 0$. The Wald chi-square statistic [= (estimate / standard error)^2] shows that p = 0.04, which is less than p = 0.05. So at an alpha level of 0.05, we can reject the null hypothesis.

Question: How do you interpret the effect of AREA of Schooling on the odds of getting admission?

Answer: Controlling for GRE and GPA, for students in rural area of schooling the odds of getting admission **multiplies** by Exp (– 0.4372) = 0.645 times compared to the students in urban area of schooling. In other words, we can say that compared to a student with an urban area of schooling, the odds of getting admission for a student with rural area of schooling is reduced by 35.5%.

This effect of area of schooling on odds of getting admission is statistically not significant and we cannot reject the Null hypothesis H_0: $\beta_{(\text{AREA of SCHOOLING})} = 0$. The Wald chi-square statistic [= (estimate / standard error)^2] shows that p = 0.1341, which is greater than p = 0.05. So at an alpha level of 0.05, we can not reject the null hypothesis.

Odds ratio Estimates for individual coefficients in a logistic regression.

Odds Ratio (Exp(β)) Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
GRE	1.002	1.000	1.005
GPA	1.949	1.031	3.688
AREA	0.645	0.364	1.144

Note that the 95% CI for odds ratio estimates of the variable “GRE “ and “GPA” does not contain 1.00, so the variables are statistically significant in predicting the odds of getting admitted in the Epidemiology program in private school. On the other hand the 95% CI of the variable “AREA” contains 1.00, and it is not statistically significant as we saw before.