ESTIMATING APPROPRIATE SAMPLE SIZE FOR RESEARCH ON MALARIA DATA: A CASE STUDY OF AFIGYA-SEKYERE DISTRICT

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DECLARATION

I hereby declare that this submission is my own work towards the Masters of Philosophy degree and that to the best of my knowledge, it contains no material previously published by another person nor material of any kind which has been accepted for the award any other degree of the university, except where due acknowledgement has been made in the context.

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ABSTRACT

Sample size determination is often important steps in planning any statistical study and is usually not easy calculating. To determine appropriate sample size it is important to use detail approach than to use short cuts. This thesis work offers distinct approaches for calculating successful and meaningful sample size for different study designs.

Additionally, there are also different procedures for calculating sample size for two (2) approaches of drawing statistical inference from the study results. That is, confidence interval and test of significance approach. Also discussed is the relationship between power and sample size estimation. Power and sample size estimations are critical steps in the design of clinical trials. Power characterizes the ability of a study to detect a meaningful significant effect if indeed it exists. Usually these tasks can be accomplished by a statistician by using estimates of treatment effect and variance or sample standard deviation from past trials or from pilot studies.

However, when exact power computations are not possible or when there is no effect size of clinical data, then simulation base approach must be adopted. This helps to recruit as many patients as required by the study than more or less patients that are not required.

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DEDICATION

I dedicate this thesis work to the Almighty Allah, my parents and my to-be wife Suhiyini Joyce Kande in appreciation for your hard support under all circumstances. Peace and blessings of God be upon you all.

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CHAPTR 1

1.0 INTRODUCTION

1.1 BACKGROUND STUDY

Despite considerable efforts throughout the century to eradicate or control malaria, it is still the most prevalent and most devastating disease in the tropics. The disease has crippling effect on the economic growth and perpetuates vicious cycles of poverty in Africa. According to United Nations Children's Fund, UNICEF (2004), it cost Africa US$10-12 billion every year in Gross domestic product even though it could be controlled for a fraction of that sum. Sagoe-Moses (2005) contended that in Africa Malaria causes approximately 20% of cerebral conditions leading to coma and death. One of the important strategies to prevent people from the risk of Malaria infection is the use of Insecticide Treated Mosquito Nets (ITMNs). The 2003 Ghana Demographic Health Survey (GDHS) revealed that among the 6251 households surveyed 17.6% had a bed net and only 3.2% had ITMNs. Recent studies have shown that the use of bed nets, especially the ITMNs may reduce both transmission and mortality by at least 25% when used properly (Sagoe-Moses 2005). It is suggested that a vast majority of household in the country do not have this simple but effective way of avoiding Malaria. The ownership distribution is not uniform; the highest ownership was recorded in the Upper East Region (25.1%). This may be attributed to the fact that UNICEF has since 2002 been distributing ITMNs at highly subsidized cost to pregnant women and children under 5 years in Northern Ghana as part of its Survival and Reproductive Health Programmes (SRHP).

In 2007, UNICEF started another strategy of supporting a pilot implementation of a new and promising Malaria prevention called "Intermittent Preventive Treatment in Infants (IPTI)".

This strategy involves the provision of curative doses of anti-Malaria, (Sulphadoxine-Pyrimethamine) to infants as they attend routine Childhood Immunization. The anti-Malaria is believed to be highly effective in reducing Malaria infection and Anaemia.

1.1.1 AFIGYE-SEKYERE DISTRICT, ASHANTI REGION, GHANA

Afigya-Sehyere district is one of the 18 administrative districts in Ashanti Region. It is bounded in the North by Sekyere West District, in the East by Sekyere East District, in the South by Kwabre District and in the West by Offinso District. Its 1998 population was estimated at 110,000 based on the 1984 census with a growth rate of 3.1%. The under 12 months and the under 5 years are 4.0% and 18.6% respectively of the population.

The health system in the district is based on Ghana's 3-tier Primary Health Care system. It is organised at 3 levels:

i. the district-led by the District Health Management Team (DHMT) with the District Director of Health Services (DDHS) as its leader,
ii. the sub-district led by the Sub-District Health Team (SDHT) based at a specified health facility and responsible for a defined geographical area and catchment population
iii. the community level - led by the Village Health Committee (VHC). The health district is divided into 6 sub-districts. It has the following health facilities: 1 district hospital (manned by the Seventh Day Adventist [SDA] Church), 5 health centers, 5 maternity clinics, 3 clinics and 1 Maternal and Chile Health centre.

The Expanded Programme on Immunisation (EPI) is one of the main activities of the Maternal and Child Health Unit of the district. Measles coverage for 1997 was 80%. The strategies used are static clinics, outreach clinics, house-to-house mop-up campaigns and

limited mass immunisation campaigns, with over 90% of infants having road-to-health cards (Browne, 1996).

The principal malaria vectors are the *Anopheles gambiae complex* and *Anopheles funestus*. Only three human plasmodia species are present: *P. falciparum* (80-90%), *P. malariae* (20-36%) and *P. ovale* (0-15%).

Malaria transmission in the district is hyper-endemic although site-specific data is lacking. In a recent unpublished study in the Ejisu-Juaben district, which shares similar ecological characteristics with the study area, *Plasmodium falciparum* parasite rates in children aged 2 - 9 years varied from 70% - 90% in the dry season in 24 communities. (Afari et al, 1992)

In a 1997 study in Afigya-Sekyere district of the Ashanti Region of Ghana, 32781 outpatient visits to hospitals were recorded. Malaria (Presumptive) accounted for 20552 visits (62.7%) with 784 Anaemia cases reported (2.3%). Admissions for 1997 were 8774. Malaria accounted for 3096 cases (35.3%) and was the leading cause of death at the district hospital. Malaria is therefore important health problems in this district. The health district therefore, provides a suitable field site for studies on Malaria control in infants in rural Ghana. (Schultz et al., 1994; Schultz et al., 1995)

1.2 PROBLEM STATEMENT

Malaria presents a serious health problem in Ghana and Afigya-Sekyere District is no exception. It is hyper- endemic with a crude parasite rate ranging from 10 – 70% and plasmodium falciparum the major malaria parasite, dominating. Although a number of statistical studies have been conducted in Afigya-Sekyere District, we want to check appropriate sample size with respect to power and significant level in this thesis work.

1.3 OBJECTIVE

1. To estimate sample sizes given significance level and power.
2. To examine the influence of sample size on the malaria data.

1.4 METHODOLOGY

Statistical research in the area of health is undertaken to obtain information for planning, operating, monitoring and evaluating health services. Central to the planning of any statistical research, is the decision on how large a sample to select from the population under study giving power and significant level, so as to help health workers and managers in making informed decision about the conduct of the research.

Hypothesis testing would be considered and power analysis would be used to test whether there is statistical effect in the sample. Data analysis was conducted using secondary data obtained from the department of community health of KNUST. The data is from a study conducted between 2002 and 2003 on children aged between 1-11years undergoing Expanded Program on Immunisation (EPI), in the Afigya-Sekyere District.

STATA and Matlab software would also be used to code simple formulae (mean and proportion) that will aid in determining sample size at various levels of significance given the effect size (the difference between two Population Parameters) and power (the probability of rejecting the null hypothesis when it is actually wrong). Information from the internet and KNUST Library is used in this research work.

1.5 JUSTIFICATION

Malaria affects everybody irrespective of one's marital status and presents significant costs to the affected households since it is possible to experience multiple and repeated attacks in a year. The cost of treatment of malaria varies according to the type of drugs given and the

length of stay in the hospital. This research work aims to stimulate increased malaria research activities in Afigya-Sekyere District in particular and in Ghana at large. A research work with reliable parameters will help in policy planning that will mitigate the spread of malaria. Thus, with good planning and reduction in malaria, the cost of treatment and waste of resources would be minimized.

Improvement in the health status of people, imply healthy workforce would be realized to grow the economy and also more children would have the opportunity to continue schooling.

1.6 THEISIS ORGANISATION

Thus, Chapter One covers Introduction of the thesis topic, Back ground of study, Problem statement, Objectives of the research, Research methodology and finally Research justification.

Chapter Two, covers Literature review and Chapter Three covers Methodology. Data analysis and findings are presented in Chapter Four. Finally Chapter Five deals with conclusions and recommendations.

CHAPTER TWO

2.0 LTERARURE REVIEW

2.1 HISTORICAL BACKGROUND

Lipsey (1990) explained that statistical studies are the best means of making inference about the population and therefore should be carefully planned. Since it would be impossible to study the entire population, conclusions about the population by sample data are without a problem. The problem should be carefully defined and operationalized. Sample unit must be selected randomly from the appropriate population of interest. The study must be of adequate size relative to the goals of the study. That is, it must be 'big enough' to detect statistical significance.

According to Shuster (1990), not all sample-size problems are the same, nor is sample size equally important in all studies. For example, the ethical issues in an opinion poll are very different from those in a medical experiment, and the consequences of an over- or under-sized study also differ. Sample size issues are usually more important when it takes a lot of time to collect the data. An agricultural experiment may require a whole growing season, or even a decade, to complete. If its sample size is not adequate, the consequences are severe.

It thus becomes much more important to plan carefully and to place greater emphasis on hedging for the possibility of under-estimating the error variance, since that would cause us to under-estimate the sample size. An under-size study exposes the subjects to potentially harmful treatment without having the capability to produce useful results, while an over-size study exposes subjects to potentially harmful treatments that use more resources than are necessary.

Odeh and Fox, (1991) argues that there are several approaches to sample size. There is sample size to achieve a specified standard error and sample size to achieve a specified

probability of obtaining statistical significance. For example, one can specify the desired width of a confidence interval and determine the sample size that achieves that goal. But the most popular approaches to sample-size determination involve studying the power of a test of hypothesis.

2.2 COX REGRESSION MODEL

Cox (1972) Regression Model is a statistical technique exploring the relationship between the survival of patients and several explanatory variables. It provides an estimate of the treatment effect on survival after adjustment for other explanatory variables. It also allows us to estimate the hazard (or risk) of death for an individual, given prognostic variables. Interpreting the Cox Regression Model involves examining the coefficients for each explanatory variable. A positive regression coefficient for an explanatory variable means that the hazard is higher and thus have worse prognosis. Conversely, a negative regression coefficient implies a better prognosis for patients with higher values of that variable.

Lagakos et al. (1978) explained that if a researcher has conducted a previous trial using different treatments A and B say, and has an estimate of the survival curve for B (S_B), the researcher can use Simpson's rule to approximate the proportion of patients that will die on treatment B:

$$d_B = \frac{1}{6}\{S_B(f) + 4S_B(f + 0.5a) + S_B(f + a)\}.$$

Where a is the accrual period and f is the followed-up period.

Also the proportion of patients that will die on treatment A can be approximated as:

$$d_A = 1 - (1 - d_B)^{\frac{1}{\Delta}}.$$

Thus, number of deaths $= (Z_\beta - Z_{1-\alpha})^2 / (P_A P_B \log_e{}^2 \Delta)$

Then the number of patients required for the trial is equal to the number of deaths divided by *d*.

$d=P_A d_A + P_B d_B$.

Julious et al. (2005) suggest that, when designing a clinical trial, an appropriate justification for sample size should be provided in the protocol. This justification could be the previous power calculation or other considerations. They argue that the greater the sample size, the smaller the standard error and consequently the greater the precision about the mean difference as assessed by its two-sided confident interval. The situation considered here is to assess with a finite sample size, what gain of precision would be realized for every unit increase in the sample size per group. A two-sided confident interval for a parallel group trial is defined as; $\bar{x}_A - \bar{x}_B \pm t_{1\alpha/2,2n-2}\sqrt{\frac{2s^2}{n}}$.

2.2.1 SAMPLE SIZE FOR THE PROPORTIONAL HAZARD REGRESSION MODEL

Schoenfeld (1981) recommended that Sample Size Formula for the Proportional Hazard Regression Model should be derived for determining the number of observations necessary to test the quantity of two survival distributions when concomitant information is incorporated. This formula should be useful in designing clinical trials with a heterogeneous patient population. He derived the asymptotic power of a class of statistics used to test the equality of two survival distributions. That result is extended to the case where concomitant information is available for each individual and where the proportional-hazards model holds. The loss of efficiency caused by ignoring concomitant variables is also computed.

According to Fleming et al. (1980) suppose that there are two treatments, A and B. The proportional-hazards model specifies that the ratio of the hazard function of a patient given Treatment B to the same patient given Treatment A will be a constant, denoted by Δ, irrespective of time or the characteristics of the patient. Thus, one parameter specifies the effect of treatment. If survival is improved more by Treatment A than by Treatment B, Δ will be greater than 1. The assumption of proportional hazards is reasonable whenever the effect of treatment is constant over time or treatment permanently affects the disease process. If treatment has a transitory effect, then tests based on the proportional-hazards model should not be used and the sample-size formula given here is not valid.

2.2.2 Sample Size Formula

Cox (1975) added that, the sample size formula for a clinical trial can be simplified if it is expressed as the number of reduction of prevalence of disease required rather than as the number of patients. Suppose that a randomised controlled trial has been designed to detect a 30% reduction in the prevalence of severe anaemia in the control group (placebo iron/placebo anti-malarial) compared with intervention group (daily iron/intermittent anti-malarial). The prevalence of anaemia in the control group is assumed to be 30%. Power is 80%, with 5% level of significance and 20% loss to follow. He states also that, one-sided test would be performed with a significance level of α and power of β when the Hazard ratio is Δ_0. Let $Z_{1-\alpha}$ and Z_β be the 1-α and β percentile of the normal distribution respectively and let P_A and P_B be the proportion of the patients randomized to treatments A and B respectively, the treatment effect would be tested by an approximate test based on partial likelihood.

Bernstein and Lagakos, (1978) suggested using approximate test based on partial likelihood to calculate sample size when two homogeneous patient groups are compared by using the F test for exponential survival, or when the logrank test is used to compare treatments with proportional hazards without covariates. However, this does not imply that covariate analysis is without benefit.

Schoenfeld, (1982) added that the formula for sample size is the same whether covariates are adjusted for or not, the powers of the two procedures are different. If the two treatment groups follow the proportional-hazards regression model, then, if covariates are ignored, the ratio of the hazard functions of the two groups will be non-proportional. This ratio will be less than Δ at every value of $t > 0$ and the power of any test without covariates will be less than that of the test that uses covariates.

2.3 VIEWS ON SAMPLE SIZE DETERMINATION

Thornley and Adams (1998) had it that one way to clarify the process of hypothesis testing is to imagine first of all a population to which no treatment have been applied and the parameters of this population (the mean and standard deviation) are known. Another population exists, that is the same as the first population, except that some treatment has been applied and the parameters are not known. Samples are drawn from later population and the statistic derived from the sample serve as the estimate of the unknown population parameter. This is the situation in which hypothesis testing is applied. Hypothesis testing begins with drawing a sample and calculating its characteristics called 'statistic', which is used to make inference about the population. The aim of hypothesis testing is usually to correctly reject the null hypothesis.

Bach and Sharpe, (1989) stated that most experimenters hope to reject the null hypothesis and therefore claim that their experimental treatment has had an effect. However, as false claims of treatment effects (type I error) are scientifically serious, it is necessary to set stringent criteria. It cannot be absolutely certain that the null hypothesis is correctly rejected or failed to be rejected but the probability associated with making an error in this process can be determined.

Snedecor and Cochran (1989) explained that, sample means very close to the population mean are highly likely and sample means distant to the population mean are unlikely but they do occur. If the null hypothesis is failed to be rejected while the treatment has no effect, it would be expected that the sample that has been drawn will have mean close to that of the population. However, sample means that have been found in the normal distribution tails indicate that the null hypothesis should be rejected. In such a case a boundary or a decision line has to be drawn therefore, between those sample means that are expected, giving the null hypothesis and those that are unlikely to lead to the rejection of the null hypothesis. That boundary is called the 'level of significance' or 'alpha level (α)'. The alpha level indicates the probability value beyond which obtained sample means are very unlikely to occur if the null hypothesis is true.

According to Cohen (1988) when testing the null hypothesis, it can be rejected when the difference between the sample data and that which would be expected according to the null hypothesis is large enough. However, if a small difference is obtained, the null hypothesis should not be accepted, instead it is failed to be rejected. He states in this case that, the researcher is according to the logic involved in this process, entitled to say that, the null is failed to be rejected.

Rejecting the null hypothesis means that the difference obtained is sufficiently unlikely to occur by chance alone and the findings were said to be statistically significant. In this case, type I error is said to be committed since there is a small chance that the conclusion is wrong. If however, the null hypothesis is not rejected the findings are not statistically significant. The null hypothesis always says that there is no treatment effect, while the alternative hypothesis says that there is treatment effect. Such statement is said to be a two-tailed hypothesis because highly unlikely events in either tail of the distribution will lead to rejection of the null hypothesis. The probability of correctly rejecting the null hypothesis is called 'the power' of the statistical test. It is large when treatment effect is large (large difference between sample data and the original population). In designing a study to maximize the power of detecting a statistically significant comparison, it is generally better, if possible, to double the effect size than to double the sample size n, since standard errors of estimation decrease with the square root of the sample size.

Muller and Benignus (1992) explained that power is calculated as 1 - β, where β is the probability of making a Type II error (failing to reject the null hypothesis when it is false). Statistical power is large when the treatment effect is large. Put another way, there is more likely to correctly reject the null hypothesis when the treatment has created a large difference between your sample data and the original population.

Other factors that influence power are:

- Sample size. Larger samples provide greater power.
- Whether a one-tailed or two-tailed test is used, statistical power is greater for one-tailed tests.
- The beta (β) level chosen. Smaller beta (β) levels produce smaller values for power.

2.4 CONCEPT OF SAMPLE SIZE DETERMINATION

Chow et al (2003) stated that numerous mathematical formulas have been developed to calculate sample size for various scenarios in clinical research based on different research objectives, designs, data analysis methods, power, type I and type II errors, variability and effect size. So order to be more accurate, sample size must be chosen such that resources and time can be well managed and that will yield interpretable results and minimizes research waste. If the sample size is too small, even a well conducted study may fail to answer its research question, may fail to detect important effects or associations, or may estimate those effects or associations too imprecisely. Similarly, if the sample size is too large, the study will be more difficult and costly, and may even lead to a loss in accuracy, effort, and research money and yields statistically inconclusive results. But Lwanga and Lemeshow, (1991) argued that sample size large enough can lead to potentially important research advances that go undetected.

Zodpey and Ughade (1999) stipulated that, medical researchers primarily consult statisticians for two reasons. Firstly, they want to know how many subjects (sample size) randomly selected should be included in their study. Secondly, they desire to attribute a p-value to their results to claim significant results. Both these statistical issues are interrelated.

If a study does not have an optimum sample size, the significant of the results in reality (true difference) may not be detected. This implies that the study would lack power to detect the significance of differences because of inadequate sample size. Whatever the outstanding results the study produces, if the sample size is inadequate their validity would be questioned.

Millard, (1987a) argues persuasively that, the ingredients in a sample size calculation for one or two groups are;

i) **Type I error (α)**: probability of rejecting the null hypothesis when it is true.

ii) **Type II error (β)**: probability of not rejecting the null hypothesis when it is false.

iii) **Power (1- β)**: probability of rejecting the null hypothesis when it is false.

iv) σ_0^2 and σ_1^2 : Variances under the null and alternative hypothesis respectively (may be homogeneous).

v) μ_0 and μ_1 means under the null and alternative hypothesis respectively,

vi) n_0 and n_1 Sample sizes in two groups (may be homogeneous).

He claims that the choice of the alternative hypothesis is challenging and that there is debate about what the null hypothesis is and what the alternative hypothesis is. His conclusion was that whatever the case, the choice affects sample size calculation and that if researchers knew the value of the alternative hypothesis, they would not need to do the study.

According to Wright (1999) in most research settings, the null hypothesis is assumed to be hypothesis of no effect and alternative hypothesis is from the researcher; "an alternative hypothesis must make sense of the data and do so with essential simplicity and shed light on other areas". This provides some challenging guidance to the selection of an alternative hypothesis. The alternative hypothesis then defines the type II error (β) and the power (1-β), while the null hypothesis provides the basis for determining the rejection region, whether the test is one or two sided and the probability of type I error (α)-the size of the test.

In survey, sampling questions to researchers are frequently addressed in terms of wanting to know a population with a specific precision. And according to Van Belle and Martin (2000), survey sampling typically deals with a finite population of size N with a corresponding reduction in the variability if sampling is without replacement. They added that, a sample of size *n* is calculated using the standard error of the sample mean ($\bar{x}$). Then the standard error of the sample mean ($\bar{x}$) is:

$$SE(\bar{x}) = \sqrt{\frac{N-n}{nN}\sigma^2}$$

The above formula reduces the standard deviation and is known as the finite population correction.

In construction management and real estate research, there are certain rules in relation to data and sample size which must be considered in the analysis. Norusis (1999) describes this analysis as Factor Analysis. He explains that the goal of factor analysis is to identify observable factors based on a larger set of observable variables. The processes are as follows:

1. The first step in factor analysis is to produce a correlation matrix for all variables. Variables that do not appear to be related to other variables can be identified from this matrix.
2. The number of factors necessary to represent the data and the method for calculating the sample size must then be determined. Principal component analysis1 (PCA) is the most widely used method of extracting factors. In PCA, linear combinations of variables are formed. The first principal component is that which accounts for the largest amount of variance in the sample, the second principal component is that which accounts for the

next largest amount of variance and is uncorrelated with the first and so on. In order to ascertain how well the model (the factor structure) fits the data, coefficients called 'factor loadings' that relate variables to identified factors, are calculated.

3. Factor models are then often 'rotated' to ensure that each factor has non-zero loadings for only some of the variables. Rotation makes the factor matrix more interpretable.
4. Following rotation, scores for each factor can be computed for each case in a sample. These scores are often used in further data analysis.

But small samples present problems in factor analysis due to splintering of factors into smaller groupings of items that really constitute a larger factor and other forms of sampling error, which can manifest itself in factors that are specific to one data set.

Result of unique patterns of responding to a single survey question, Costello and Osborne (2005*a*) report two extreme problems in factor analysis; the Heywood effect (in which the impossible outcome of factor loadings greater than 1.0 emerge) and the failure to produce a solution, were only observed in small samples. The failure to produce a solution occurred in almost one third of analyses in the smallest sample size category. They empirically tested the effect of sample size on the results of factor analysis reporting that larger samples tend to produce more accurate solutions (70% of the samples with the largest *N:p* ratio (20:1) produced correct solutions).

2.5 SAMPLE SIZE DETERMINATION FOR SAMPLE MEAN AND PROPORTION

Wunsch (1986) is holding the view that researchers use information gathered from survey to generalize findings from a drawn sample back to a population within the limits of drawn error.

They do consider single Mean and Proportion as well as difference in Means and proportions and Power. However, when analysing business education research, two of the most consistent flaws include;

1) Disregard for sampling error when determining sample size.

2) Disregard for response and non-response bias.

But Holton and Burnette (1977) argued that within a quantitative survey design determining sample size and dealing with non-response bias is essential.

2.6 SAMPL SIZE AND POWER

Sample size and power calculations are often based on a two-group comparison. However, in some cases the group membership cannot be ascertained until after the sample has been collected. According to Rowe et al. (2006), to conduct sample size calculations for the two-group case, a researcher needs to specify the outcome of interest (Proportion for binary response) to be used in estimating the sample size, the group variances, the desire power, the type I error rate, the number of sides of the test and the ratio of the two-group sizes and that the desired power must be sufficient. This is because in clinical studies, without sufficient power, the study can fail to detect a significant effect when it exists. This consideration must be well balanced with the high cost of recruiting and evaluating large samples of subjects, thus making power calculations a crucial step in designing clinical research studies.

2.6.0 MEAN AND PROPORTION METHOLOGY

2.6.1 MEAN

Kraemer and Thiemann (1987) believed that the clearest reason why statistical analyses are based on the means of samples instead of single values is that they are more reliable when it comes to estimation of population parameter. In relative terms the sample statistic is used to estimate population parameter. Suppose we are trying to estimate populations mean value μ from data $x_1,.....,x_n$, a random sample of size n. The quick estimate of (μ), the population mean, is the sample mean, ($\bar{x}$). Similarly the sample variance (S^2) is used to estimate the population variance (σ^2). In broader terms the sample becomes more precise estimate of the population mean as the sample size (*n*) increases.

A quantitative measure of this precision is the standard error, $\frac{\sigma}{\sqrt{n}}$, which decreases as the precision increases and the vice versa. The larger *n* becomes the smaller the standard error becomes.

According to Lachin (1981), the dependence of standard error on the sample size can be exploited at the planning stage. The investigator decides how much precision is needed for this purpose and designs the study accordingly. Sample size could be based directly on the measure of precision so that the width of a confident interval or the size of the standard error is required to be at most a prescribe value. Alternatively, sample size can be determined by setting a hypothesis test with a giving power. The latter is probably more widely used by researchers than the former. It is most important to ensure that the right standard error is used otherwise the sample size (*n*) might not be optimum.

The same applies to difference between means of two groups. A limit is set for the standard error of the difference between the means of the two groups.

If the response in the two groups have a common standard deviation, then the standard error of $\bar{x}_1 - \bar{x}_2$ is: $s\sqrt{\frac{1}{n_1}+\frac{1}{n_2}}$, where s estimates the common standard deviation and n_1, n_2 are the sizes of the two groups.

Another case cited by Machin et al. (1997), on sample size calculation when comparing means of samples. In this case the researcher question is whether the new treatment works when compared to placebo; (Prevention trial). He wants to find out how many patients with mild hypertension would need to be recruited into a trial, in order to detect an average difference of 5mm Hg in systolic blood pressure, between an intervention group who receive a new anti-hypertensive and a control group (who effectively receive delayed intervention). He assumes the standard deviation of systolic blood pressure is 10mmHg, 90%power and 95%confident interval (5%significant level). And also standard difference (effect size) is Δ. In the case of two means, μ_1 and μ_2, the number of patients with mild hypertension is estimated as;

$$n = \frac{2 \times [Z_{(1-\alpha/2)} + Z_{\beta}]^2}{\Delta^2}$$

2.6.2 PROPORTION

Guilford (1954*a*) reported that, proportion in sampling describes a case in which the occurrence of an event is of interest to a researcher. The researcher may be interested in establishing that the proportion of a sample response to a treatment.

Like the mean, a researcher can determine sample size using proportion either by confidence interval or hypothesis testing.

Within the confident interval, sample size can be achieved by specifying the standard error. To demonstrate this, it must be ensured that the population proportion from which the sample proportion is to be selected randomly is normally distributed.

Guilford (1954*b*) also reported that the sample proportion is not known until the study is complete. For research purposes, researchers get values for $\hat{p}$ from previous studies or pilot studies. Otherwise, $\hat{p}$ is assumed to be 1/2 or (0.5), because the bigger $\hat{p}$ (1- $\hat{p}$) is, the larger *n* has to be. And $\hat{p}$ (1- $\hat{p}$) takes its biggest value at $\hat{p}$ = 0.5. He estimated the proportion of the population who support the death penalty (under a particular question wording) where the population proportion is suspected to be around 60%. He first considered the goal of estimating the true proportion *p* to accuracy (standard error) to be at least 0.05 or 5 percentage points, from a simple random sample of size *n*. The standard error of the proportion is $\sqrt{p(1-p)/n}$. Substituting the guessed value of 0.6 for *p* yields a standard error of $\sqrt{0.6\times 0.4/n} = 0.49/\sqrt{n}$, and so we need $0.49/\sqrt{n} \le 0.05$ or $n \ge 96$. More generally, we do not know *p,* so we would use a conservative standard error of $\sqrt{0.5\times 0.5/n} = 0.5/\sqrt{n}$, so that $0.5/\sqrt{n} \le 0.05, or\ n \ge 100$.

Mace (1964) claimed that, Hepatitis B is rated as the fourth biggest killer among the world infectious diseases. He wanted to take a sample of citizens of a particular city to determine the percentage of people who have Hepatitis B by way of using confidence interval.

He assumes that if *n* is large enough and confidence interval for the true proportion *P* is given by $\hat{p} \pm Z^{*}se(\hat{p})$.

The interval has width (w), which is twice the margin of error. This expression involves $\hat{p}$ which is unknown until the study is finished. Suppose the margin of error is to be at most *m*.

Then $n \geq \left(\frac{Z}{m}\right)^2 \times \hat{p}(1+\hat{p})$. (1994 World Health Organization)

The above equation depends on $\hat{p}$ which is unknown when planning the survey. However, taken $\hat{p} = 0.5$ makes $\hat{p}(1-\hat{p})$ biggest for larger *n*. This shows that huge samples are needed to estimate proportions very precisely.

Altman, (1990) stated that for intervention trial (comparing new treatment with an existing one) the researcher's challenge is to determine whether the new treatment will work better than the existing one. With standard therapy 40% of patients on average, achieve a favourable outcome (e.g. single-layer compression stockings for the treatment of venous leg ulcer). It is anticipated that a new treatment (e.g. Multi-layer compression stockings) will increase the 'cure' rate to 50%. He explained that with 80% power at a 5% level of statistical significance, the sample size required in each intervention group can be obtained using test of hypothesis. Where $Z_{1-\alpha/2}$ *and* $Z_{1-\beta}$ represent percentage points of the normal distribution for statistical significance level and power respectively.

According to Costello and Osborne (2005*b*), demonstrating that more than half the population supports a death penalty, then the appropriate sample size to achieve a specified probability of obtaining statistical significance using hypothesis that p >1/2 is based on the

estimate $\hat{p} = \frac{x}{n}$ from a sample of size *n*. This will be evaluated under the hypothesis that the true proportion is p = 0.60, using the conservative standard error for $\hat{p}$ of $\sqrt{0.5 \times 0.5 / n} = 0.5 / \sqrt{n}$.

This is however, mistaken because it confuses the assumption that $p = 0.6$ with the claim that $\hat{p} > 0.6$. In fact, if $p = 0.6$, then $\hat{p}$ depends on the sample, and it has an approximate normal distribution with mean 0.6 and standard deviation $\sqrt{0.6 \times 0.4 / n} = 0.49 / \sqrt{n}$.

Cohen (1988) found that to determine the appropriate sample size, the desired power and the interval level (the conventional level of power and interval level in sample size calculations is 80% and 95% respectively) must be specified. That is, 80% of the possible 95% confidence intervals will not include 0.5 and the probability that a 95% interval will be entirely above the comparison point of 0.5. When the sample size (*n*) is increased, the estimate becomes closer (on average) to the true value, and the width of the confidence interval decreases.

CHAPTER 3

INTRODUCTION

3.1 SAMPLE SIZE DETERMINATION TECHNIQUES

Sample size calculation is very important for research studies where samples are required. If the research population size is large, then the costs involved in collecting data from all subjects would automatically be high. In this respect, the sample means ($\bar{x}$) becomes better estimate of the population mean (μ) as the sample size increases. The reasons why statistical analysis are based on means of samples is that they make more sense. If a conclusion can be drawn from a small sample size that has the power to detect any statistically significant effect, then recruiting more than necessary subjects will be unnecessary since it has the tendency not only to cause financial and management problems but it raises ethical concerns.

Determining the sample size for a study is a crucial component of study design. The goal is to include sufficient numbers of subjects so that statistically significant results can be achieved. In this study simple formulae are provided for the sample size determination for both mean and proportion. For simplicity, formulae are expressed in terms of hypothesis testing for both mean and proportion. This is necessitated in the medical field by Epidemiologists, where a treatment group is compared with a control (an intervention) group to test the efficacy of a new drug on a particular ailment. The Epidemiologist will then have to determine the number of patients required for both groups (the new drug and placebo) that can detect any statistical difference if it exists. Since the levels of almost any attributes exhibits variability, then the treatment group values will exhibit some level of variability, likewise the control group.

Many statistical analyses grapple with this problem-giving that if it is known that subjects will vary in their responses to the same treatment, then the observed difference between treatment groups would be consistent to state with relative certainty that the treatment worked, (Faraday, 2006). When an epidemiologist is planning a clinical trial, it is very important to consider how many participants will be needed to reliably answer the clinical question. One of the most important decisions to make before calculating a sample size is to define a clinically important treatment effect, δ (or delta), which should not be confused with a statistically significant treatment effect. Of course, since researchers are embarking on a study, new intervention would be expected to be an improvement of previous intervention, such that the difference can be estimated realistically. In other words, to estimate the difference is to consider whether the observed treatment effect would make the current clinical practice change. For example, if the new intervention was looking at a treatment to lower blood pressure, the researcher might argue that an average lowering of systolic BP of 5mm Hg is clinically important; however, the researcher might decide that an average lowering of systolic BP of 10mm Hg would be clinically important and necessary before he would possibly think about prescribing this treatment.

The number of participants required depends on four (5) parameters. These are:

(1) Statistical Power levels

(2) P-value

(3) Statistical Significance Level

(4) Treatment variability

(5) Error variability

Statistical power is the probability of detecting treatment effect if it exists. Beta (β) is defined as false-negative rate and power as 1- β. Power should be stated such that it can optimally detect treatment effect. Adequate power for a trial is widely accepted as 0.8 (or 80%) probability of detecting treatment effect, Cochran (1977).

P-value measures consistency between the results actually obtained in the trial and the "pure chance" explanation for those results. It is used to test a null hypothesis against an alternative hypothesis using a data set. In other words, P-value is a probability value quantifying the strength of the evidence against the null hypothesis in favor of the alternative hypothesis. It has been recommended that the size of the P-value be used as a measure of the evidence against the null hypothesis. A similar approach, but which has a slightly different emphasis, is to reject the null hypothesis if the P-value is below some critical value, *C*. According to Cochran (1977), the critical value is set generally at 0.05 or 5% probability of detecting significant difference which will occur by chance.

In determining appropriate sample size, parameters such as statistical significant level, alpha (α), typically 5% is sometimes written α =0.05, power written = 1- β, P-value, population mean (μ) population proportion (P) are to be considered. For the first three parameters, that is statistical significant, power and p-value can be pre-determined and the rest are estimated. Thus, the researcher can estimate them by using pilot studies, relevant literature or rule-of-thumb.

The standard deviation, which usually comes from previous research or pilot studies, is often used for the response variable.

Pilot studies is said to be the most accurate calculation of sample size in that relevant data will be collected on pilot basis from which an estimate of treatment and error variability can be made.

It is however, worth noting that the results of a pilot study need not necessarily be statistically significant in order for the data to be used to estimate treatment and error variability. This procedure is the first best method of calculating sample size.

Another way to calculate appropriate sample size by way of estimating treatment and error variability is the used of relevant literature. This estimate can be achieved by means of published work of investigators who have conducted similar studies. This is the second best method of calculating sample size.

The last means of estimating treatment and error variability is the rule-of-thumb. This is accepted if and only if data or published works are absent. In fact this is the least accurate means of calculating sample size. In general if the variability associated with the treatment is large relative to the error, then relatively few subjects will be required to obtain statistically significant results.

On the other hand, if the variability associated with the treatment is small relative to the error then, relatively more subjects will be required to obtain statistically significant results. (Faraday, 2006)

In the valuation of new drugs and vaccine, treatments are in general allocated randomly to individual subjects and methods for the design and analysis of such trials are well established.

According to Faraday (2006), many such trials have been conducted over different occasions and times.

These include: a series of trials of the impact of insecticides-treated bed-nets on child mortality in Africa in which treated nets were randomized to villages and other geographical areas, a trial of the impact of improved treatment services for sexually-transmitted diseases (STD) on the incident of HIV infection in which rural communities in Ghana were randomly assigned to intervention or control groups and a trial of a smoking cessation intervention in which communities in Ghana were assigned randomly to intervention or control groups. The most commonly encountered clinical trial scenario is the comparison of two equal-sized studied groups where the primary outcomes are either proportions (e.g. percentage responding to treatment) or means (e.g. average blood pressure). A number of previous reports have discussed sample size calculations for such trials most of which focused on the variable of interest on either the mean or the proportions. It is often possible to perform such calculations using available standard statistical software packages for this purpose.

3.2 SAMPLE SIZE FOR COX REGRESSION MODEL

In clinical trials, there is a period of observation within which the subject is censured. Thus the data typically consists of censored failure times where the censoring time may also differ among the subjects; such censoring techniques arise when subjects quit the study at various. The censoring time is considered to occur at random in certain studies. The model described below is known as Cox Regression Model (CRM).

$h(t; x) = h_0(t)\exp\{\beta_1 x_1 + \ldots\ldots\ldots + \beta_k x_k\}$ …… (1)

where h $(t; x)$ is the hazard function at time t for a subject with covariate values x_1,…….., x_k, h_0 is the baseline hazard function when all covariate equal to zero,

β_i is the regression coefficient for the ith covariate, x_i.

Statistical analysis of failure-time data is an active and important area of research that has received considerable attention from several applied disciplines. Historically, failure times are modeled by fitting an exponential, or log normal distribution to the data. It is shown that the formula for the sample size that requires the comparison of two groups with exponential curves is valid when Proportional Hazard Regression Model (PHRM) is used to adjust for covariates. A patient hazard function will depend on the treatment he or she receives as well as the characteristics of the patient. If patients have a decrease probability of death after they survive past the first or second year, then the hazard function decreases. On the other hand, in long-term studies the hazard function increases as age increases the probability of death.

The formula below is used to calculate appropriate sample size when two homogeneous patient groups are compared.

$n = (Z_\beta + Z_{1-\alpha})^2/(P_A P_B \log_e{}^2\Delta)$…… (2)

where n is number of deaths,

β and α are power and significant level respectively,

$Z_{1-\alpha}$ and Z_β are percentile of the normal distribution respectively,

Δ is hazard ratio,

P_A and P_B are the proportion of the patients randomized to treatments A and B respectively.

(Bernstein and Lagakos, 1978)

Cox's method is similar to multiple regression analysis, except that the dependent (*Y*) variable is the hazard function at a given time. If we have several explanatory (*X*) variables of interest (for example, age, sex and treatment group), then we can express the hazard or risk of dying at time *t* $h(t)=h_o(t)\exp(\beta_i xi)$

as: $h(t) = h_0(t)\ x\ \exp(b_1 age + b_2.sex + ... + b_3.group)$

The regression coefficients b_1 to b_3 give the proportional change that can be expected in the hazard, related to changes in the explanatory variables. They are estimated by statistical method called maximum likelihood, using an appropriate computer program (for example, SAS, SPSS or STATA). [Freeman et al, 2008]

The Cox Regression Model (CRM) or Proportional Hazard Model since 1992 has become a statistical theory of counting process that unifies and extends nonparametric censored survival analysis. It provides an estimate of effect on survival after adjustment for other explanatory variables. In addition, it allows us to estimate the hazard (or risk) of death for an individual, given their prognostic variables. The approach integrates the benefits on nonparametric approaches to statistical inferences. The data in CRM includes (T_i, Z_i), i = 1, 2,…… n,

where n is the number of observations in the study,

T_i is the time of failure of the ith observation,

Z_i is the p-dimensional vector of covariates.

We continue by providing simple sample size formulae for both continuous and categorical data.

3.3 CATEGORICAL DATA

Formula and procedure for determining sample size for categorical data are very similar to that of continuous data. Assuming that Cochran's formula is to be used for the calculation of sample size with *t* significant level, *p* proportion and $\underline{d}$ margin of error, then;

$$\underline{n}_0 = \frac{(\underline{t})^2 \times (p)(q)}{(\underline{d})^2}$$

where q= (1-p)

Supposing the population size (N) is known and the sample size calculated ($\underline{n}_0$) is greater than 5% of N, that is $\underline{n}_0 > N \times 0.05$, then the researcher will resort to use Cochran's correction formula below;

$$\underline{n}_1 = \frac{\underline{n}_0}{\left(1 + (\underline{n}_0 / population)\right)}$$

TABLE: 3.1 STATISTICAL TABLE FOR SIGNIFICANCE LEVEL AND POWER

Significance level			Power			
5%	1%	0.1%	80%	85%	90%	98%
1.96	2.5758	3.295	0.8416	1.0364	1.2816	1.6449

Illustrative Example;

Suppose a researcher has set significant level t=0.05,

an estimated proportion *p*=0.5,

q=0.5 and an estimated standard deviation *d*=0.05

then:

$$\underline{n}_0 = \frac{(1.96)^2 \times (0.5) \times (0.5)}{(0.05)^2} = 384$$

If N=1679, then $N \times 0.05$=84.

This is less than the calculated sample size $\underline{n}_0$.

So using the Cochran's 1977 correction formula

$$\underline{n}_1 = \frac{384}{(1 + 384/1679)} = 313$$

This is the minimum returned sample size required.

3.4 CONTINUOUS DATA

Before a researcher proceed with sample size calculation using continuous data, the researcher determines if categorical variable will play primary role in the data analysis. If it can, then sample size formula for categorical data is used. Otherwise, sample size formula below propounded by Cochran (1977), for continuous data is appropriate.

$$\underline{n}_0 = \frac{(\underline{t})^2 \times (\underline{s})^2}{(\underline{d})^2}$$

Assuming the population size (*N*) is known and the sample size calculated ($\underline{n}_0$) is greater than 5% of *N*, that is $\underline{n}_0 > N \times 0.05$, then the researcher will use Cochran's correction formula below;

$$\underline{n}_1 = \frac{\underline{n}_0}{\left(1 + (\underline{n}_0 / population)\right)}$$

Illustrative Example;

Suppose a researcher has set significant level $\underline{t}$=0.05

acceptable margin of error estimated for mean $\underline{d}$ =0.21,

an estimated standard deviation in the population $\underline{s}$ = 1.167.

then;

$$\underline{n}_0 = \frac{(1.96)^2 \times (1.167)^2}{(0.21)^2} = 118$$

For population *N*=1679, the required sample size is 118.

However, since this sample size exceeds 5% of the population (1,679*.05=84), Cochran's (1977) correction formula is used to calculate the final sample size.

This calculation is as follows:

$$\frac{118}{(1+118/1679)} = 111$$

These procedures result in the minimum returned sample size.

However, as alpha (α) level decrease from 5% to say 1% and the acceptable margin of error increases from 5% to say 10%, the sample size calculated is said to be significant foe any giving population and therefore, Cochran's correction formula is not applicable in this case.

3.5 PROPORTIONS

In this research like most research, the objective is to compare the proportions of two groups (intervention and control). Assume that π_0 and π_1 are the estimated sample proportions of the true population proportions in the intervention and the control group respectively. Also assume that $Z_{\alpha/2}$ and Z_β are percentage points of the normal distribution for statistical significance level and power, respectively. Then for individually-randomized trials, standard formula requires a total of *n* individuals in each group is expressed as follows;

$$\pi_0 = (Z_\beta + Z_{\alpha/2})\sqrt{\frac{\pi_0(1-\pi_0)}{n_0}},$$

$$\pi_1 = (Z_\beta - Z_{\alpha/2})\sqrt{\frac{\pi_1(1-\pi_1)}{n}},$$

$$(\pi_0 - \pi_1) = (Z_\beta - Z_{\alpha/2})\sqrt{\frac{\pi_0(1-\pi_0)}{n_0}} + (Z_\beta + Z_{\alpha/2})\sqrt{\frac{\pi_1(1-\pi_1)}{n_1}}$$

Assume that $n_0=n_1=n$

$$(\pi_0 - \pi_1) = (Z_\beta - Z_{\alpha/2})\left[\sqrt{\frac{\pi_0(1-\pi_0)+\pi_1(1-\pi_1)}{n}}\right]$$

$$\sqrt{n} = (Z_\beta + Z_{\alpha/2})\left[\sqrt{\pi_0(1-\pi_0)+\pi_1(1-\pi_1)}\right]/(\pi_0 - \pi_1)$$

$$\therefore n = (Z_\beta + Z_{\alpha/12})^2[\pi_0(1-\pi_0)+\pi_1(1-\pi_1)]/(\pi_0 - \pi_1)$$

This is the required sample size for each group a researcher will consider to find out whether there is a significant difference between the two groups (intervention and placebo). Suppose we sought to calculate sample size of citizens of a particular community to determine the percentage of people who are carrying a given diseases.

Suppose also that 95% confidence level of precision is required. Assuming the sample size *n* is large enough, then the confident interval for the true proportion *p* by;

$\hat{p} \pm Z * se(\hat{p})$,

where $se(\hat{p})$ is the standard error of the true proportion and is given as; $se(\hat{p}) = \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$

If the distribution is normally and randomly selected, then the interval will have width; $w = 2 \times Z_{\alpha/2}\sqrt{\hat{p}(1-\hat{p})/n}$

The expression which involves $\hat{p}$ is unknown until the study is complete.

Now let E= $Z_{\alpha/2}\sqrt{\hat{p}(1-\hat{p})/n}$,

where *E* is the margin of error.

Suppose the researcher wants E to be no more than a certain value, say *b*, then is E ≤ *b*.

$Z_{\alpha/2}\sqrt{\hat{p}(1-\hat{p})/n} \leq b$

Squaring both sides and making *n* the subject, we have

$n \geq \left(\frac{Z}{b}\right)^2 [\hat{p}(1-\hat{p})]$

From the above equation we realized that *n* depends eventually upon $\hat{p}$ which is unknown initially and also the size of $\hat{p}(1-\hat{p})$ depends on $\hat{p}$. When $\hat{p}(1-\hat{p})$ is larger, then *n* is also larger. As the case may be $\hat{p}(1-\hat{p})$ takes its largest value when $\hat{p}$ =1/2 or 0.5.

The plot of $\hat{p}(1-\hat{p})$ versus $\hat{p}$ to gives Figure 3.1 below

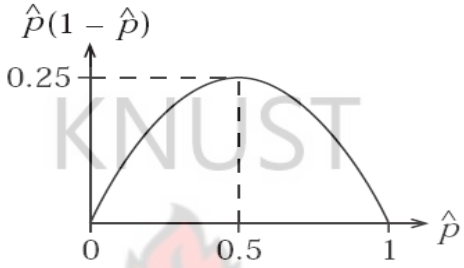


Figure 3.1: Plot of $\hat{p}(1-\hat{p})$ against $\hat{p}$

If we use 95% confident interval, that is z=1.96, *b*=0.025, $\hat{p}$ = 0.5, then

$n \geq \left(\frac{1.96}{0.025}\right)^2 \times (0.5)(0.5)$ =1536.64. Rounding it up would probably end up taken 1500 or 2000 depending upon the budget.

NB: Use $\hat{p}$ =1/2 unless it is known that $\hat{p}$ belongs to an interval k ≤ $\hat{p}$ ≤ m that does not include1/2, in this case substitute the interval endpoint nearer to 1/2 for $\hat{p}$. (Hirano, K., and J.R. Porter. 2008).

According to (Fleiss, 1981; Shuster, 1999) if 0.2 ≤ $\hat{p}$ ≤ 0.6 or 0.4 ≤ $\hat{p}$ ≤0.9, substitute $\hat{p}$ = 0.5.

If it is known that 0.02 ≤ $\hat{p}$ ≤ 0.10, substitute $\hat{p}$ = 0.1, and if 0.7 ≤ $\hat{p}$ ≤ 0.9, substitute $\hat{p}$ = 0.7.

These calculations are applicable only when researchers seek to get the require precision for single proportion estimates. As researchers increase confidence for $\hat{p}$ and increase the width of the confident interval, *n* becomes larger. On the other hand, when holding width and the confidence interval constant and decrease $\hat{p}$ then *n* decreases. But larger numbers are needed to get precisions for differences. However, researchers often use sample less than one thousand people for reason of cost and difficulty in controlling biases. It is very difficult to reducing sampling error base on the level of biases. (Cohen, 1977)

3.6 COMPARISON OF TWO PROPORTIONS

3.6.1 **Intervention Trial Example**

In epidemiological studies, comparison of two proportions is quite common. Here the objective is to compare two treatment groups (those living on new treatment and those on old treatment) to find out if there is any treatment effect.

An epidemiologist would be required to calculate an appropriate sample size that can detect the treatment if it exists. Suppose that the number of patients in each group is *n*,

then:

$$n = \frac{2 \times [Z_{(1-\frac{\alpha}{2})} + Z_{(1-\beta)}]^2}{\Delta^2},$$

$$\Delta = \frac{p_1 - p_2}{\sqrt{\bar{p}(1-\bar{p})}},$$

$$\bar{p} = \frac{(p_1 + p_2)}{2}$$

where $Z_{(1-\alpha/2)}$ and $Z_{(1-\beta)}$ represent percentage points of the normal distribution for statistical significance level and power respectively,

Δ is the standardize difference,

n is the required sample size for each group

p_1 and p_2 are the two proportions

$\overline{p}$ is the average of the two proportions

Illustrative Example:

With standard therapy, 40% of patients, on average, achieve a favorable outcome (e.g. single layer compression treatment of ordinary stomach ulcers). It is anticipated that a new treatment (e.g. multi-layer compression) will increase the 'cure' rate to 50%.

What sample size would be required in order to detect such a treatment effect with 80% power at a 5% level of significance?

First calculate Δ, the standardized difference. In the case of two proportions, p_1 and p_2,

p_1=0.50 (or 50%), p_2=0.40 (or 40%) and so $\overline{p} = \frac{(0.5+0.4)}{2} = 0.45$

Hence $\Delta = \frac{(0.5-0.4)}{\sqrt{0.45\times(1-0.45)}} = \frac{0.10}{\sqrt{0.45\times 0.55}} = \frac{0.10}{0.2475} = \frac{0.10}{0.46749} = 0.201$

Using the values from the table for 5% level of significance, $Z_{(1-\alpha/2)}$ = 1.96, and 90% power, $Z_{(1-\beta)}$ = 1.2816.

Then,

$n = \frac{2\times(1.96+1.2816)^2}{(0.201)^2} = \frac{2\times(3.2416)^2}{(0.201)^2} = \frac{2\times(10.50797056)}{0.0404} = \frac{21.01594112}{0.0404} = 520.2$

Rounding up to the nearest whole number and say that 521 participants are required per treatment group or 1042 in total.

In the medical environment the outcome measure of most interest at the end of the study will be dichotomous; yes or no, dead or alive, improve or not improve.

Suppose a medical researcher wishes to design a study to compare two treatment groups with respect to the proportion of successes in each using two-sided test. The hypothesis is,

$H_0 : p_1 - p_2 = 0$ $H_1 : p_1 - p_2 \neq 0$.

Let us assume that $p_2 > p_1$, an effect size $(ES) = p_2 - p_1$. Assume also that both proportions p_2 and p_1 have the common sample size, $n_1 = n_2 = n$, then the appropriate sample size (n);

$$n = \frac{p_1(1-p_1) + p_2(1-p_2)}{(p_2 - p_1)^2} \times (Z_\alpha + Z_\beta)^2$$

If the population proportion is normally distributed and the test statistic for both samples is Z, then;

$Z = \frac{\hat{p}_2 - \hat{p}_1}{\sqrt{2\overline{pq} \times (1/n)}}$, where $\overline{p} = \frac{\hat{p}_2 + \hat{p}_1}{2}$ and $\overline{q} = 1 - \overline{p}$.

Under the null hypothesis (H_0), power = 1-β =P ($|Z| > Z_{\alpha/2} / H_0$ false) then $\frac{\hat{p}_2 - \hat{p}_1}{\sqrt{2\overline{pq} \times (1/n)}}$ $> Z_{\alpha/2}$ is the rejection region.

Under the alternate hypothesis (H_1) the effect size (ES) is $p_2 - p_1$ and the standard deviation is $\sqrt{\frac{p_1 q_1 + p_2 q_2}{n}}$ instead of $\sqrt{\frac{2\overline{pq}}{n}}$, since $p_1 - p_2 \neq 0$. Now Z which is normally distributed $= \frac{|\hat{p}_2 - \hat{p}_1 - ES|}{\sqrt{\frac{p_1 q_1 + p_2 q_2}{n}}}$. Thus $\hat{p}_2 - \hat{p}_1 = Z\sqrt{\frac{2\overline{pq}}{n}}$ and so $Z = \frac{Z\sqrt{\frac{2\overline{pq}}{n}} - ES}{\sqrt{\frac{p_1 q_1 + p_2 q_2}{n}}}$

Now P ($|Z| > Z_{\alpha/2} / H_0$ false) becomes

$$P\left[\frac{Z\sqrt{\frac{2\overline{pq}}{n}}-ES}{\sqrt{\frac{p_1q_1+p_2q_2}{n}}} > \frac{Z_{\alpha/2}\sqrt{\frac{2\overline{pq}}{n}}-ES}{\sqrt{\frac{p_1q_1+p_2q_2}{n}}} \;\middle|\; H_1 \text{ true}\right]$$

But $$\frac{Z_{\alpha/2}\sqrt{\frac{2\overline{pq}}{n}}-ES}{\sqrt{\frac{p_1q_1+p_2q_2}{n}}} = Z_\beta$$

$$Z_{\alpha/2}\sqrt{\frac{2\overline{pq}}{n}} - ES = \sqrt{\frac{p_1q_1+p_2q_2}{n}} \times Z_\beta$$

$$ES = Z_{\alpha/2}\sqrt{\frac{2\overline{pq}}{n}} + \left(-Z_\beta\sqrt{\frac{p_1q_1+p_2q_2}{n}}\right).$$

Squaring both sides;

$$(ES)^2 = Z^2{}_{\alpha/2}\frac{2\overline{pq}}{n} + \frac{(p_1q_1+p_2q_2)}{n}Z^2{}_\beta$$

$$\therefore \quad n = \left[\frac{Z^2{}_{\alpha/2}(2\overline{pq}) + (p_1q_1+p_2q_2)Z^2{}_\beta}{(ES)^2}\right].$$

By some transformations,

$$n_i = \left[\frac{Z_{\alpha/2}\sqrt{2\overline{pq}} + Z_\beta\sqrt{p_1q_1+p_2q_2}}{ES}\right]^2.$$

where the sample size for each group is n_i .

3.7 METHOD BASED ON ESTIMATION

The confidence interval for a mean is $\bar{x} \pm t * s/\sqrt{n}$,

where *s* is the sample standard deviation,

t is the appropriate point from a *t*-distribution.

The value of *t* changes with *n* once *n* > 30. Consequently it is much simpler to base sample size calculation on the approximate confident interval $\bar{x} \pm z * s/\sqrt{n}$, where Z is the appropriate point of a standard normal distribution. If the calculation results in a value of *n* below 30 then it might be prudent to increase the value slightly to allow for this approximation. If the standard error required is to be less than a certain value, say *L* then *n* must exceed S^2/L^2.

Also if the value of *s* is unknown, it can be replaced by σ if it is known. In case σ is not known, it is appropriate to use values from either pilot studies or previous literature and then *n* must exceed σ^2/L^2. It is important to ensure that the correct standard error is used. The formula $\bar{x} \pm z * s/\sqrt{n}$, uses the standard error of the sample mean $[se(\bar{x}) = s/\sqrt{n}]$. If the standard error is meant for the difference between means of two groups with common standard deviation then the standard error of $\bar{x}_1 - \bar{x}_2$ is;

$S\sqrt{1/n_1 + 1/n_2}$, where *S* estimates the common standard deviation, n_1 and n_2 are the sizes of the groups. Suppose the standard error of the two groups is required to be at most a given value, say L, then;

$L \geq S\sqrt{1/n_1 + 1/n_2}$. Recall that $n_1 = n_2 = n$.

$$L \geq S\sqrt{\frac{1+1}{n}} = S\sqrt{\frac{2}{n}}$$

$$L^2 \geq \frac{2S^2}{n}$$

$\therefore n \geq 2S^2/L^2$. This is the sample size for each group.

3.8 METHOD BASED ON HYPOTHESIS TESTS

In hypothesis testing of two means, the null hypothesis of is that the two population means are equal ($\mu_1 = \mu_2$) and the alternative hypothesis is that the two population means are not equal ($\mu_1 \neq \mu_2$).

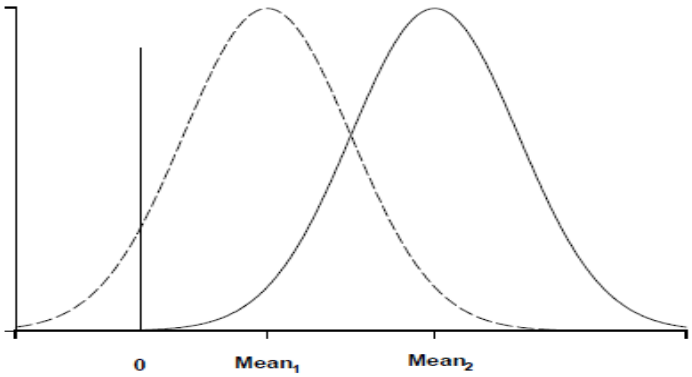
It is assumed that the responses in the two groups share a common population standard deviation. Two errors are said to be committed in this case; type I error (rejecting the true hypothesis) and type II error (failing to reject the false hypothesis). The probability of committing type I error does not depend on *n* but on critical value and the probability of committing type II error depends on *n*.

We set $\mu_1 - \mu_2 = 0$ for null hypothesis and $\mu_1 - \mu_2 \neq 0$ for alternative hypothesis. We know that $\bar{x}_1 - \bar{x}_2$ is an imprecise estimate but contains information on $\mu_1 - \mu_2$.

Consider these two cases in which one $\mu_1 - \mu_2$ (1) has a giving value and the other $\mu_1 - \mu_2$ (2) has a value twice the previous and both cases have the same standard deviation. The observed values of $\bar{x}_1 - \bar{x}_2$ in the two cases are shown in the figure below:

Figure 3.2 below indicates the distributions of the observed values $\bar{x}_1 - \bar{x}_2$. The dashed curve has a mean μ_1 and the solid curve has a mean μ_2 . This concludes that $\mu_1 - \mu_2 \neq 0$ since the solid curve has twice the population mean of the dashed curve. In other words, $2\mu_1 = \mu_2$.

As $(\mu_1 - \mu_2)/se$ gets larger the solid curve moves to the right, so the chance of not rejecting the null hypothesis gets smaller.



Difference between groups

Figure 3.2: distribution of different sample means ($\bar{x}_1, \bar{x}_2$)

A second circumstance to consider is when there are two cases, where the difference in the population means is the same in both cases but the standard errors are different. This is shown in figure 3.3 below.

Solid curve has half the standard error of the dashed curve but both have the same mean.

It is clear that we have a much better chance of inferring that $\mu_1 - \mu_2$ is non-zero in the case with the smaller standard error. The standard error depends on the sample size and it can be made as small as possible by making the sample size sufficiently large. If the standard error is sufficiently small, then the distribution of $\bar{x}_1 - \bar{x}_2$ will be clustered sufficiently tightly about $\mu_1 - \mu_2$ that (provided $\mu_1 - \mu_2$ really is not zero) it will be very likely to be able to infer that $\mu_1 - \mu_2 \neq 0$. This is the basis of using this approach to set sample sizes.

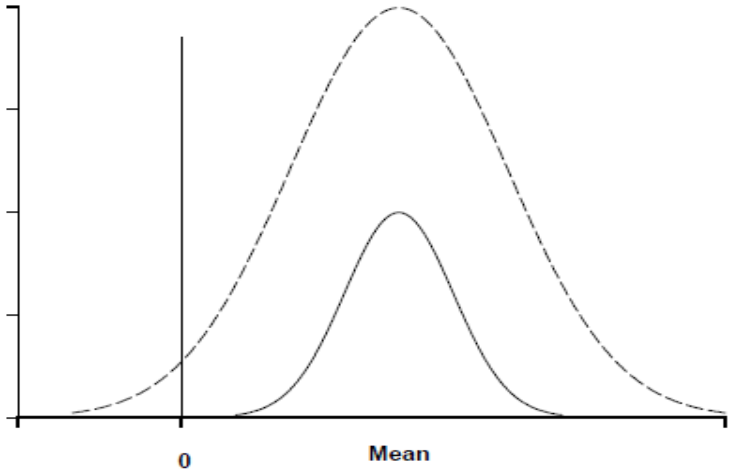


Figure 3.3: distribution of the same sample mean

3.8.1 **Sample Size Formula**

Suppose a researcher is comparing two groups of studies, with the responses in both groups having a normal distribution with the same standard deviation (σ) but different means, μ_1 and μ_2 respectively. A test of the null hypothesis that these means are equal will have Type II error β (so power 1-β).

The null and the alternate hypothesis here are:

$H_0 : \mu_1 = \mu_2$, $H_1 : \mu_1 \neq \mu_2$

Where μ_1 and μ_2 are the population means for the two groups, assume that the population variance is the same for both groups. If the same number of subjects is to be used in each group then the appropriate test statistic is given as; $Z = \frac{\bar{x}_1 - \bar{x}_2}{\sigma} \times \frac{\sqrt{n}}{\sqrt{2}}$

where $\bar{x}_1$ and $\bar{x}_2$ are the average weight gains observed in the two groups and Z is the test statistic of the normal distribution. The null hypothesis is rejected in favour of the alternative if; $Z > Z_\alpha$

where Z_α is the appropriate normal deviate.

The type II error, β is defined to be; β = p (accept H_0 / H_1 false) = p (Z< Z_α / H_1 false).

If H_1 is true then Z has a normal distribution with mean given by; $\mu = \frac{\mu_1 - \mu_2}{\sigma} \times \frac{\sqrt{n}}{\sqrt{2}}$ and standard deviation equal to one.

Consequently $Z_\beta = Z_\alpha - \mu$

So that $\beta = \int_{-\infty}^{Z_\alpha - \mu} \frac{1}{\sqrt{2\pi}} e^{-x^2/2} dx$.

Additionally $\beta = \int_{-\infty}^{Z_\beta} \frac{1}{\sqrt{2\pi}} e^{-x^2/2} dx$.

$-Z_\beta = Z_{\alpha/2} - (\mu_1 - \mu_2)/se$

where $se = \sigma\sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$

$n_1 = n_2 = n$

Leading to $\frac{\mu_1 - \mu_2}{\sigma} \times \frac{\sqrt{n}}{\sqrt{2}} = Z_\alpha + Z_\beta$

That implies $\sqrt{n} = \frac{\sqrt{2}(Z_\alpha + Z_\beta)\sigma}{(\mu_1 - \mu_2)}$, and therefore $n = \frac{2\sigma^2 (Z_{\alpha/2} + Z_\beta)^2}{(\mu_1 - \mu_2)^2}$.

The problem with this approach is the choosing of values for σ and $(\mu_1 - \mu_2)$. If there is little or no past data on the studies for the chosen response variable it may be impossible to choose appropriate value for both σ and $(\mu_1 - \mu_2)$. It is important to be clear how to think of the value of $\mu_1 - \mu_2$. (Cohen, 1977; Kraemer and Thieman, 1982)

The choice of α and β, type I and type II error rates respectively, is on the researcher. But σ and $(\mu_1 - \mu_2)$ need to be obtained whether from the literature, existing data or design pilot study.

As $\mu_1 - \mu_2$ gets larger, either positively or negatively, the probability of rejecting the null hypothesis approaches 1. However, if $\mu_1 - \mu_2$ =0 then the probability of rejecting the null hypothesis is fixed at 0.05 (or, more generally, α), so the curves for all tests, whatever sample size they use, must pass through the point (0, 0.05). At a given value of $\mu_1 - \mu_2$ (strictly $\mu_1 - \mu_2 / \sigma$), the higher curve in figure 3.4 corresponds to the larger sample sizes. Sample size is larger in dashed case than solid.

It is remarked that the power of a test was a function of $\mu_1 - \mu_2$ and this is made explicit in figure 3.4.

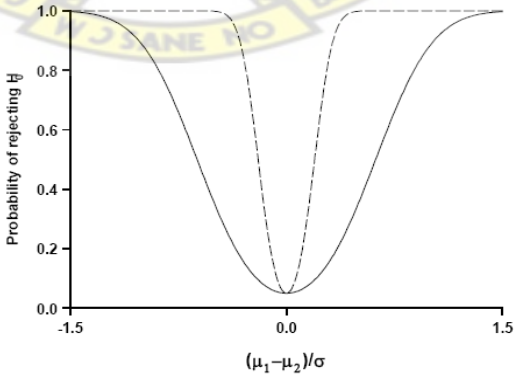


Figure 3.4: power curves for two tests

3.9. MEAN

Sample sizes could be based directly either on the measure of precision so that the size of a standard error is required to be less than a prescribe value or the sample size could be set so that a hypothesis test have a giving power. A numerical measure of this precision is the standard error, $\sigma/\sqrt{n}$ which decreases as the precision increases. It is important to realize that sample size calculation do not give exact values, they depend on the values of the unknown parameter (population mean; population standard deviation) and therefore will vary as the values used for the parameters vary.

Then, $\mu_0 = (Z_{\frac{\alpha}{2}} + Z_\beta)\sqrt{\frac{\sigma_0^{\,2}}{n_0}}$,

$\mu_1 = (Z_{\frac{\alpha}{2}} + Z_\beta)\sqrt{\frac{\sigma_1^{\,2}}{n_1}}$,

$(\mu_0 - \mu_1) = (Z_{\frac{\alpha}{2}} + Z_\beta)\sqrt{\frac{\sigma_0^{\,2}}{n_0}} + (Z_{\frac{\alpha}{2}} + Z_\beta)\sqrt{\frac{\sigma_1^{\,2}}{n_1}}$

Assume that $n_0 = n_1 = n$

$(\mu_0 - \mu_1) = (Z_{\frac{\alpha}{2}} + Z_\beta)\left[\sqrt{\frac{\sigma_0^{\,2} + \sigma_1^{\,2}}{n}}\right]$

Then $\sqrt{n} = (Z_{\frac{\alpha}{2}} + Z_\beta)\left[\sqrt{\sigma_0^{\,2} + \sigma_1^{\,2}}\right]/(\mu_0 - \mu_1)$

$\therefore \quad n = (Z_{\frac{\alpha}{2}} + Z_\beta)^2\left[\sigma_0^{\,2} + \sigma_1^{\,2}\right]/(\mu_0 - \mu_1)^2$

3.10 COMPARISON OF TWO MEANS

3.10.1 **Prevention trial example**

In epidemiological study, comparison of two proportions is more often than comparison of two means. This is because clinical or public health decisions are based on clear outcome and less on the difference of the mean values.

For instance, an epidemiologist may want to administer treatment and placebo on patients and would want to find out the number of patients for each group that should be recruited in the study in order to achieve effectiveness. If this is so, then

$$n_i = \frac{2 \times (Z_{(1-\frac{\alpha}{2})} + Z_{(1-\beta)})^2}{\Delta^2}$$

Where i=1, 2 and n_1=n_2

$\Delta = \frac{\mu_1 - \mu_2}{s}$, is the standard difference

$(\mu_1 - \mu_2)$ is the effect size (ES), and s is the common standard deviation

Illustrative example:

An epidemiologist wants to find out how many patients with mild hypertension would need to be recruited in a trial in order to detect an average difference $(\mu_1 - \mu_2)$ of 5$mmHg$ in systolic blood pressure between the treatment group and the placebo group, assuming the standard deviation (s) of systolic blood pressure is 10$mmHg$, 98% power, and 1% level of significance.

$$\Delta = \frac{5mmHg}{10mmHg} = 0.5$$

$Z_{(1-\alpha/2)} = 2.5758, \quad Z_{(1-\beta)} = 1.6449$

Then $n_i = \frac{2(2.5758+1.6449)^2}{(0.5)^2} = \frac{2(4.2207)^2}{0.25}$

$n_i = 142.5 \approx 143$ for each group.

Also suppose a researcher wants to design a study such that two treatment groups can be compared with respect to the means which are two-sided test and are normally distributed. Then the hypothesis is that;

$H_0 : \mu_2 - \mu_1 = 0$

$H_1 : \mu_2 - \mu_1 \neq 0$.

If $\mu_2 > \mu_1$, then the effect size (ES) = $\mu_2 - \mu_1$.

Let $n_1 = n_2 = n$, and $\sigma_1^2 = \sigma_2^2$.

If Z is the test statistic and, $\bar{x}_1$ and $\bar{x}_2$ are estimates for μ_1 and μ_2 respectively,

then under the null hypothesis (H_0);

$$Z = \frac{|\bar{x}_2 - \bar{x}_1|}{\sqrt{\frac{2\sigma^2}{n}}} \quad \text{..... (3.1)}$$

Power (1- β)= $p(Z > Z_{1-\alpha/2} / H_0$ is false). If $Z > Z_{1-\alpha/2}$ it means that the variable of interest is within the rejection region and therefore H_0 is false.

Since n_1=n_2=n, then under the alternative hypothesis the common standard error

$$D = \sqrt{\frac{\sigma_1^2 + \sigma_2^2}{n}},$$

The test statistic now becomes;

$$Z= \frac{\left|\bar{x}_2 - \bar{x}_1\right| - ES}{\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}} \quad \ldots\ldots (3.2)$$

From (3.1) $\left|\bar{x}_2 - \bar{x}_1\right| = Z\sqrt{\frac{2\sigma^2}{n}}$, so (3.2) becomes $Z = \frac{Z\sqrt{\frac{2\sigma^2}{n}} - ES}{\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}}$.

Then power = 1-β = P$\left[\frac{Z\sqrt{\frac{2\sigma^2}{n}} - ES}{\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}} > \frac{Z_{\alpha/2}\sqrt{\frac{2\sigma^2}{n}} - ES}{\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}} \;\middle|\; H_0 \textit{false} \right]$.

We want to say that $Z_\beta = \frac{Z_{\alpha/2}\sqrt{\frac{2\sigma^2}{n}} - ES}{\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}}$, this implies

that $Z_{\alpha/2}\sqrt{\frac{2\sigma^2}{n}} - ES = Z_\beta\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}$.

Implies $ES = Z_{\alpha/2}\sqrt{\frac{2\sigma^2}{n}} + \left(-Z_\beta\sqrt{\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}}\right)$,

Squaring both sides,

$$(ES)^2 = Z^2{}_{\alpha/2}\frac{2\sigma^2}{n} + Z_\beta{}^2\left(\frac{\sigma_1^{\,2} + \sigma_2^{\,2}}{n}\right)$$

$$n(ES)^2 = Z_{\alpha/2}2\sigma^2 + Z_\beta{}^2(\sigma_1^{\,2} + \sigma_2^{\,2})$$

$$\therefore \quad n = \frac{Z^2{}_{\alpha/2}(2\sigma^2) + Z_\beta{}^2(\sigma_1^{\,2} + \sigma_2^{\,2})}{(ES)^2}.$$

By some transformations $n_i = \left[\frac{Z_{\alpha/2}\sqrt{2\sigma^2} + Z_\beta\sqrt{\sigma_1^{\,2} + \sigma_2^{\,2}}}{ES}\right]^2$

where the sample size for each group is n_i.

According to Mark Woodward (1999) and Altman (1990), as power increases say from 80% to 90%, sample size increases and the more likely one is to detect a treatment effect if it exists.

CHAPTER 4

4.0 DATA ANALYSIS AND RESULTS

4.1 PARAMETERS OF STUDY ON SULFADOXINE/PLACEBO FROM AFIGYA-SEKYERE DISTRICT

This chapter focuses on analysis of study data from Afigya-Sekyere District of the Ashanti Region in 1998. The trial was designed to detect a 30% reduction in the prevalence of malaria in the intervention group (sulfadoxine) compared with control group (placebo anti-malaria). The prevalence of malaria in the control group was assumed to be 30%. Power was 80% with 5% level of significance and 20% loss to follow. The objective was to determine the effect of intermittent malaria treatment in infancy at risk of malaria.

The 1998 population of Afigya-Sekyere District was estimated at 110,000 based on the 1984 census with children with at most one year being 4, 400. The sample size for the total population of children within that year group was estimated at 900 in total. The method used was continuous enrolment of infants for a period of 12 months. During the study, all infants who came for Maternal and Child Health (MCH) clinic were recruited after informed consent was given by mother and the inclusion criteria were met. Details of children who are permanent resident of Afigye-Sekyere District and those who are not resident as well as other relevant information were recorded in a chart sheet. Infants recruited into the study were randomised into one of the two trial groups (Control/ Intervention) and a computer generated random number were assigned to each individual. Mothers were provided information on their next clinic date for collection of monthly supply of sulfadoxine or placebo. Field workers made monthly visits to homes of study infants to check on compliance with sulfadoxine/placebo supplementation and replenish supplies.

4.2 ANALYSIS IN SAMPLE SIZE DETERMINATION

Since the study was aimed at protecting infants against prevalence of malaria in Afigya-Sekyere-District where the prevalence of malaria is assumed to be 60%, they were put on two treatment groups, A (placebo) and B (sulfadoxine), trial. The trial was designed to detect 30% reduction in the prevalence of malaria in the intervention group (sulfadoxine) compared with the control group (placebo). The prevalence of malaria in the control group is assumed to be 30%. Power is 80% with 5% level of significance and 20% loss to follow. The sample size used, based on these assumptions was 450 infants per group (900 infants in total). Assume that the two treatments, A (Placebo) and B (Sulfadoxine) are administered.

Let P_A = proportion of infants randomized on treatment A

P_B = proportion of infants randomized on treatment B

Δ = ratio of the hazard function

4.3 SUMMARY OF DATA FROM AFIGYA-SEKYER DISTRICT

Prevalence of malaria in infants on placebo was

P_A= 0.3 or

P_A = 30%

Expected prevalence of malaria reduction in infants on sulfadoxine was 30%.

Therefore, the actual prevalence for P_B was [30% - (1/3×30%)]

Therefore, P_B = 20% or

P_B= 0.2

$\Delta = 0.15$

Duration of study =12 months

Total sample size for both arms= 900 (450 for each of two arms)

$Z_{(1-\alpha/2)}$ = value for 95% confidence interval

Z_{β} = value for 80% power

Then according to Fleming *et* al. (1980) the formula for appropriate sample size for the proportional hazard function is given by

$$n = (Z_{(1-\alpha/2)} + Z_{\beta})^2 / (P_A P_B \log^2{}_e \Delta).$$

The hazard function was coded using STATA software and the results of the STATA analysis are shown in tables 4.1 and 4.3. Where $Z_{(1-\alpha/2)}$ = 95%, $\Delta = 0.15$, P_B are constants and Z_{β}, P_A, were varied with prevalence.

From the STATA software, table 4.1 below shows prevalence percentages of malaria in column 2, the power in column 1. For each prevalence there correspond two outcomes (No parasite and Parasite present) with each outcome relating to two variables, the number of infants on placebo (n_A) and the number of infants on sulfadoxine (n_B), where the total sample size for each variable is distributed randomly among the outcomes. Total sample size for each prevalence is displayed in column six (6). The purpose of this table is to generate total sample size for each percentage prevalence for a given power.

Table 4.1: SAMPLE SIZE DISTRIBUTION OF TREATMENT GROUPS FOR INFECTED AND NON-INFECTED INFANTS

POWER	PERCENTAGE		VARIABLES		
		Malaria	**Placebo(n_a)**	**Sulfadoxine(n_b)**	**Total**
80%	**30%**	No Parasite	12 (44.4%)	14 (66.7%)	26 (54.2%)
		Parasite Present	15 (55.6%)	7 (33.3%)	22 (45.8%)
		Total	27 (100%)	21 (100%)	48 (100%)
	40%				
		No Parasite	43 (49.4%)	79 (73.8%)	122 (62.9%)
		Parasite Present	44 (50.6%)	28 (26.2%)	72 (37.1%)
		Total	87 (100%)	107 (100%)	194 (100%)
	50%				
		No Parasite	43 (49.4%)	72 (72.7%)	115 (61.8%)
		Parasite Present	44 (50.6%)	27 (27.3%)	71 (38.2%)
		Total	87 (100%)	99 (100%)	186 (100%)
85%	**30%**				
		No Parasite	14 (45.2%)	16 (69.6%)	30 (55.6%)
		Parasite Present	17 (54.8%)	7 (30.4%)	24 (44.40%)
		Total	31 (100%)	23 (100%)	54 (100%)
	40%				
		No Parasite	47 (49.5%)	94 (74.0%)	141 (63.5%)
		Parasite Present	48 (50.5%)	33 (26.0%)	81 (36.5%)
		Total	95 (100%)	127 (100%)	222 (100%)
	50%				
		No Parasite	47 (50.5%)	89 (73.6%)	136 (63.6%)
		Parasite Present	46 (49.5%)	32 (26.4%)	78 (36.4%)

		Total	93 (100%)	121 (100%)	214 (100%)
90%	**30%**				
		No Parasite	16 (44.4%)	17 (65.4%)	33 (53.2%)
		Parasite Present	20 (55.6%)	9 (34.6%)	29 (46.8%)
		Total	36 (100%)	26 (100%)	62 (100%)
	40%				
		No Parasite	55 (50.0%)	109 (72.7%)	164 (63.1%)
		Parasite Present	55 (50.0%)	41 (27.3%)	96 (36.9%)
		Total	110 (100%)	150 (100%)	260 (100%)
	50%				
		No Parasite	52 (49.5%)	105 (72.4%)	157 (62.8%)
		Parasite Present	53 (50.5%)	40 (27.6%)	93 (37.2%)
		Total	105 (100%)	145 (100%)	250 (100%)
98%	**30%**				
		No Parasite	22 (50.0%)	22 (68.8%)	44 (53.6%)
		Parasite Present	22 (50.0%)	10 (31.2%)	32 (46.4%)
		Total	44 (100%)	32 (100%)	76 (100%)
	40%				
		No Parasite	59 (46.5%)	143 (74.1%)	202 (63.1%)
		Parasite Present	68 (53.5%)	50 (25.9%)	118 (36.9%)
		Total	127 (100%)	193 (100%)	320 (100%)
	50%				
		No Parasite	58 (47.5%)	135 (73.4%)	193 (63.1%)
		Parasite Present	64 (52.5%)	49 (26.6%)	113 (36.9%)
		Total	122 (100%)	184 (100%)	306 (100%)

Table 4.2 below shows percentage prevalence in column 1 and proportion in column 2 ($Proportion = \frac{prevalence}{100}$).

4.2 Percentage Prevalence and Corresponding Proportion

Prevalence	Proportion
30%	0.3
40%	0.4
50%	0.5

It is observed from Table 4.2 that for a given prevalence, there corresponds a given proportion.

Table 4.3 below is an extract from Table 4.1 and it shows the STATA computed sample size corresponding to a given prevalence and power.

Table 4.3: Distribution of Sample Sizes for a given Prevalence and a given Power

		Power			
		80%	85%	90%	98%
Prevalence	30%	48	54	62	76
	40%	194	222	260	320
	50%	186	214	250	306

It is observed from Table 4.3 that for a given power (say 80%) the sample size follows a concave curve as prevalence increase from 30% to 50%.

Figures 4.1 to 4.4 below are the graphical representations of the sample size variation as observed in Table 4.2.

Sample sizes are plotted on the vertical axis and Prevalence Rates on horizontal axis for the various powers.

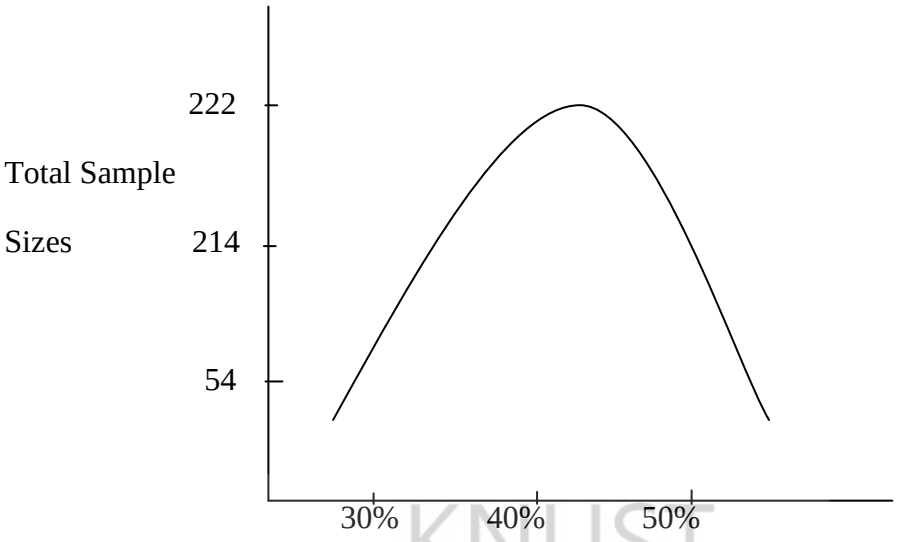


Figure 4.1: Plot of Total Sample Sizes against Prevalent Rates for 80% Power.

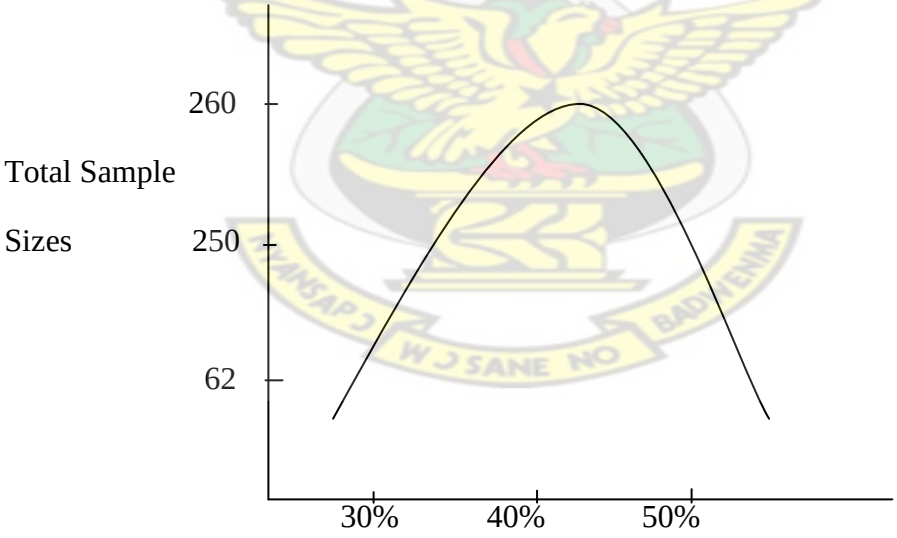


Figure 4.2: Plot of Total Sample Sizes against Prevalent Rates for 85% Power

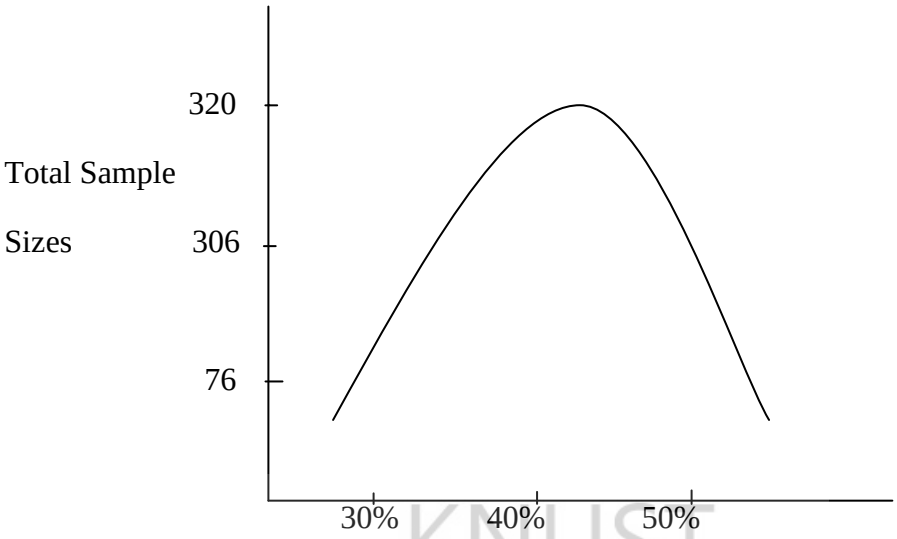


Figure 4.3: Plot of Total Sample Sizes against Prevalent Rates for 90% Power

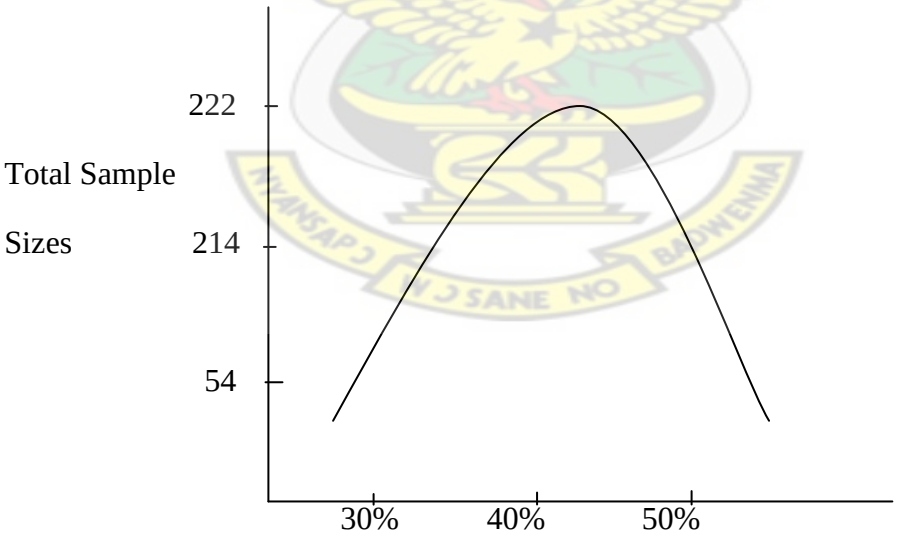


Figure 4.4: Plot of Total Sample Sizes against Prevalent Rates for 98% Power

From Figures 4.1 to 4.4 it is observed that at a certain prevalence, sample size reaches its peak and any further increase in prevalence corresponds to decrease sample size.

4.4 ESTIMATING TOTAL SAMPLE SIZE WITH THE LEAST INTERVAL WIDTH USING POWER ANALYSIS

A well powered sample size should have the least interval width for a particular confidence interval and for a given prevalence percentage (Odeh et al., 1991). For the 1998 study in Afigya-Sekyere District, prevalence percentage was 30% with 80% power and a total sample size of 900.

Table 4.4 below is used to analyse the effectiveness of the study. It shows power in column 1; prevalence percentage of malaria in column 2; sample sizes (*n*) in column 3; STATA generated Hazard Ratio at 95% confidence interval in column 4 and interval width in column 5 (the difference between numbers in bracket in column 4 give the interval width). For each power there corresponds various prevalence rates each relating to a sample size and an interval width. The aim of this table is to obtain at a given power a sample size and corresponding prevalence percentage that has the least interval width 95% confidence interval.

Table 4.4: POWER ANALYSIS

Power	Prevalence	*n*	Hazard Ratio (95%CI)	Interval Width
80%	30% 40% 50%	48 194 186	0.79(0.40,1.55) 0.87(0.63,1.20) 0.89(0.67,1.23)	1.15 0.57 0.56
85%	30% 40% 50%	54 222 214	0.94(0.51,1.73) 0.90(0.66,1.21) 0.86(0.63,1.17)	1.22 0.55 0.54
90%	30% 40% 50%	62 260 250	1.09(0.65,1.85) 0.91(0.86,1.22) 0.87(0.65,1.16)	1.20 0.36 0.51
98%	30% 40% 50%	76 320 306	1.01(0.63,1.63) 1.04(0.80,1.35) 1.02(0.78,1.32)	1.00 0.55 0.54

Table 4.5a below is extracted from Table 4.4 and it shows the STATA computed sample size corresponding to a given power and prevalence. It shows the various powers in column 2; the various prevalence in row 2 and varying sample sizes in columns 3 to 5.

Table 4.5a: Distribution of Sample Sizes for a given Power and a given Prevalence

		Prevalence		
		30%	40%	50%
Power	80%	48	194	186
	85%	54	222	214
	90%	62	260	250
	98%	76	320	306

It was observed in Table 4.5a that as power increases the corresponding sample size increases for a given prevalence rate (say 30%).

Table 4.5b below is also extracted from Table 4.1 and shows power in column 1; prevalence percentage in column 2; interval width in column 3 and sample size in column 4. The table illustrates the prevalence percentage and sample size that corresponds to the minimum interval width for each power.

Table 4.5b: Appropriate Sample Sizes

POWER	RATE (%)	INTERVAL WIDTH	SAMPLE SIZE (*n*)
80%	50	0.56	184
85%	50	0.54	214
90%	40	0.36	260
98%	50	0.54	306

It was observed that as power was increasing the corresponding sample size was also increasing for a given prevalence rate. But this pattern did not show in the interval width. For effectiveness of research, researchers seek to use the characteristic of sample size with the smallest interval width (Odeh et al., 1991). From Table 4.5b above the smallest interval width is 0.36 which occurs at sample size of 260 with expected prevalence rate of 40% and of power 90%.

Table 4.5b shows that at a particular prevalence of 50% using power of 85% for research instead of increased power of 98% gives the same interval width and therefore the same efficiency of research. However, the sample size to be used (306) at 98% is greater than (214) at 85% power. Since increased sample size cost more for the research activities, the lack of corresponding efficiency means it is better to use power of 85% and the sample size of 214 for such a research if 50% prevalence is to be expected. This confirms Cochran (1977) contribution that, large sample size corresponding to high power does not necessarily mean that it can detect any significance difference. Sample size which is well powered and has the smallest interval width is reasonable enough to detect any significance difference if it exists.

4.3 DISCUSSION OF RESULTS

This study revealed that for a given power sample size is a concave curve function of expected prevalence rate. For the same prevalence rate and interval width the power corresponding to a lower sample size is preferred.

For 1998 study in Afigya-Sekyere District a sample size of 520 (260 for each of the two arms) at 90% prevalence should be used with prevalence of 40%. It is observed from Table 4.5b that as power increases the corresponding sample size increases for a given prevalence rate.

The Literature shows that different methods of calculating sample size should be used for different experimental designs.

For single mean and single proportion the maximum error formula could be used.

For difference in means and proportions formula for hypothesis testing could be used.

Tables and figures on the use of these formulae are found in appendix 6 to 19.

CHAPTER 5

5.0 CONCLUSION AND RECOMMENDATION

5.1 CONCLUSION

This thesis work covered the basic discussions for estimating sample size given significance level and power, and for examining the influence of sample size on malaria data in Affigye-Sekyere District.

It addresses the position of power and its relationship to sample size and interval width. It was revealed in Table 4.5a that as power was increasing sample size was also increasing for a given prevalence rate. But the pattern deviates in Table 4.5b for interval width.

For the 1998 study in Afigya-Sekyere District a sample size of 520 (260 for each of the two arms) at 90% confidence interval should be used since that is has the least interval width of 0.36 with prevalence of 40%.

The STATA analysis used in this thesis was based on the hazard function since the Afigya-Sekyere study used survival analysis.

The research revealed that different methods of calculating sample size could be used for different experimental designs. For single mean and single proportion the maximum error formula could be used, and for difference in means and proportions formula for hypothesis testing could be used.

5.2 RECOMMENDATION

It is usual for researchers to have different opinions as to how sample size should be calculated. The procedures used in this thesis work are comprehensive enough to narrow the different opinions researchers have. Well powered studies estimate reasonable sample sizes where cost of studies is saved at the end. In order to obtain a more realistic sample size estimate, it is appropriate for researchers to simulate data on survival distribution. Models like Monte Carlo simulation could be used to estimate appropriate sample size.

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APPENDICES

APPENDIX_1

CODES FOR SAMPLE DETERMINATION USING SINGLE PROPORTION

```
function table=SampleSizeDetSingleProp(p_cap,E)

Z_Alpha_on_2=[1.64 1.96 2.5758];q_cap=1-p_cap;

table=cell(2,length(Z_Alpha_on_2)+1);%Create a matrix of strings to contain the Z and n
values

table{1,1}='Z_Alpha/2';table{2,1}='n';%1st row 1st colum contain 'Z_Alpha_on_2',

                    %2nd row 1st colum contain 'n'

for i=1:length(Z_Alpha_on_2)%For every element of Z_Alpha_on_2

n(i)=ceil(p_cap*q_cap*(Z_Alpha_on_2(i)/E)^2);%Find n

end

for i=2:length(Z_Alpha_on_2)+1%From the 2nd column onwards

table{2,i}=n(i-1);;%Let the 2nd row, ith column of the table be i-1th element of n

table{1,i}=Z_Alpha_on_2(i-1);%Let the 1st row, ith column of the table be i-1th elementof
Z_Alpha_on_2

end

xlswrite('SampleSizeDetSingleProp.xls',table)
```

APPENDIX_2

CODE FOR SAMPLE DETERMINATION USING DIFFERENCE IN PROPORTION

```
function table=SampleSizeDetDiffProp(p1,p2)

Z_beta=[0.84161.03641.28161.6449];Z_Alpha_on_2=1.64;%[1.64 1.96 2.5758];

table=cell(length(Z_Alpha_on_2)+1,length(Z_beta)+1);%Create a matrix of strings to contain the Z and n values

table{1,1}='Z_Alpha/2/Z_beta';%1st row 1st colum contain 'Z_Alpha_on_2' and 'Z_beta'

q1=1-p1;q2=1-p2;ES=abs(p2-p1);p_bar=(p1+p2)/2;q_bar=1-p_bar;

for i=1:length(Z_Alpha_on_2)%For each element of Z_Alpha_on_2

for j=1:length(Z_beta)%For each element of Z_beta

n(i,j)=ceil(((Z_Alpha_on_2(i)*sqrt(2*p_bar*q_bar)+Z_beta(j)*sqrt(p1*q1+p2*q2))/ES)^2)
;%Find n(i,j)

end

end

plot(n,Z_beta)%Plot n against Z_beta

xlabel('n');ylabel('Power')%Label the x and y axes as n and power respectively

legend('Z_{\alpha/2}=1.64')%Indicate a description of the plot

for i=2:length(Z_Alpha_on_2)+1%From the 2nd row onwards

for j=2:length(Z_beta)+1%From the 2nd column onwards
```

```
table{i,j}=n(i-1,j-1);%Let the ith row, jth column entery of table be the i-1th row, j-1th column %element of n

table{1,j}=Z_beta(j-1);%Let the 1st row jth column entery of table be the j-1th element of Z_beta

end

table{i,1}=Z_Alpha_on_2(i-1);%Let the ith row, 1st column entery of table be thei-1th element of Z_Alpha_on_2

end

xlswrite('SampleSizeDetDiffProp.xls',table)
```


APPENDIX_3

CODES FOR SAMPLE DETERMINATION USING SINGLE MEAN

```
function table=SampleSizeDetSingleMean(Sigma,E)

Z_Alpha_on_2=[1.64 1.96 2.5758];

table=cell(2,length(Z_Alpha_on_2)+1);%Create a matrix of strings to contain the Z and n values

table{1,1}='Z_Alpha/2';table{2,1}='n';%1st row 1st colum contain 'Z_Alpha_on_2',
  %2nd row 1st colum contain 'n'

for i=1:length(Z_Alpha_on_2)

n(i)=ceil(Sigma^2*(Z_Alpha_on_2(i)/E)^2);%For every value of Z_Alpha_on_2 calculate %which is and integer

end

for i=2:length(Z_Alpha_on_2)+1%For the remaining columns

table{2,i}=n(i-1);          %Put the i-1 n value in the 2nd row and ith column

table{1,i}=Z_Alpha_on_2(i-1);%Put the i-1 Z_Alpha_on_2 value in the 1st row and ith column

end

xlswrite('SampleSizeDetSingleMean.xls',table)%Write the table in excel withthe name SampleSizeDetSingleMean.xls
```

APPENDIX_4

CODES FOR SAMPLE SIZE DETERMINATION USING DIFFERENT MEANS BUT COMMON SIGMA

```
function table=SampleSizeDetSameSigma(Mu_1,Mu_2,Sigma)

Z_beta=[0.84161.03641.28161.6449];

Z_Alpha_on_2=1.64;

table=cell(length(Z_Alpha_on_2)+1,length(Z_beta)+1);%Create a matrix of strings to contain the Z and n values

table{1,1}='Z_Alpha/2/Z_beta';%1st row 1st colum contain 'Z_Alpha_on_2' and 'Z_beta',

for i=1:length(Z_Alpha_on_2)%For every value of Z_Alpha_on_2

for j=1:length(Z_beta) %For every value of Z_beta

n(i,j)=ceil(2*Sigma^2*(Z_Alpha_on_2(i)+Z_beta(j))^2/(Mu_1-Mu_2)^2);%Find n which is an integer

end

end

for i=2:length(Z_Alpha_on_2)+1%For the 2nd row onwards

for j=2:length(Z_beta)+1%For the 2nd column onwards

table{i,j}=n(i-1,j-1);%Let the ith row, jth column entery of table be thei-1th row, j-1th column entry of n
```

```
table{1,j}=Z_beta(j-1);%Let the 1st row, jth column of the table be the j-1th element of Z_beta

end

table{i,1}=Z_Alpha_on_2(i-1);%Let the ith row, 1st column of the table be the element of Z_Alpha_on_2

end

plot(n,Z_beta)%Plot n against Z_beta

xlabel('n');ylabel('Power')%Label the x and y axes as n and Power respectively

legend('Z_{\alpha/2}=1.64')%Indicate a description of the plot

xlswrite('SampleSizeDetSameSigma.xls',table)
```

APPENDIX_5

CODES FOR SAMPLE SIZE DETERMINATION USING DIFFERENCE IN MEANS AND DIFFERENT SIGMA

```
function table=SampleSizeDetDiffSigma(Mu_0,Mu_1,Sigma_0,Sigma_1)

Z_beta=[0.84161.03641.2816 1.6449];Z_Alpha_on_2=1.96;%[1.64 1.96 2.5758];

table=cell(length(Z_Alpha_on_2)+1,length(Z_beta)+1);%Create a matrix of strings to containthe Z and n values

table{1,1}='Z_Alpha/2/Z_beta';%1st row 1st column contain 'Z_Alpha_on_2' and 'Z_beta'

for i=1:length(Z_Alpha_on_2)%For every element of Z_Alpha_on_2

for j=1:length(Z_beta)%For every element of Z_beta

n(i,j)=ceil((Z_Alpha_on_2(i)+Z_beta(j))^2*(Sigma_0^2+Sigma_1^2)/(Mu_0-Mu_1)^2);%Find n

end

end

plot(n,Z_beta)%Plot n against Z_beta

xlabel('n');ylabel('Power')%Label the x and y axes as n and Power respectively

legend('Z_{\alpha/2}=1.96')%Indicate a description of the plot

for i=2:length(Z_Alpha_on_2)+1%From the 2nd row of the table onwards

for j=2:length(Z_beta)+1%From the 2nd column  of the table onwards
```

table{i,j}=n(i-1,j-1);%Let the ith row, jth column entry of the table be thei-1th row, j-1th column element of n

table{1,j}=Z_beta(j-1);%Let the 1st row, jth column of entry of the table be j-1th element of Z_beta

end

table{i,1}=Z_Alpha_on_2(i-1);%Let the ith row, 1st column entry of table be i-1th element Z_Alpha_on_2

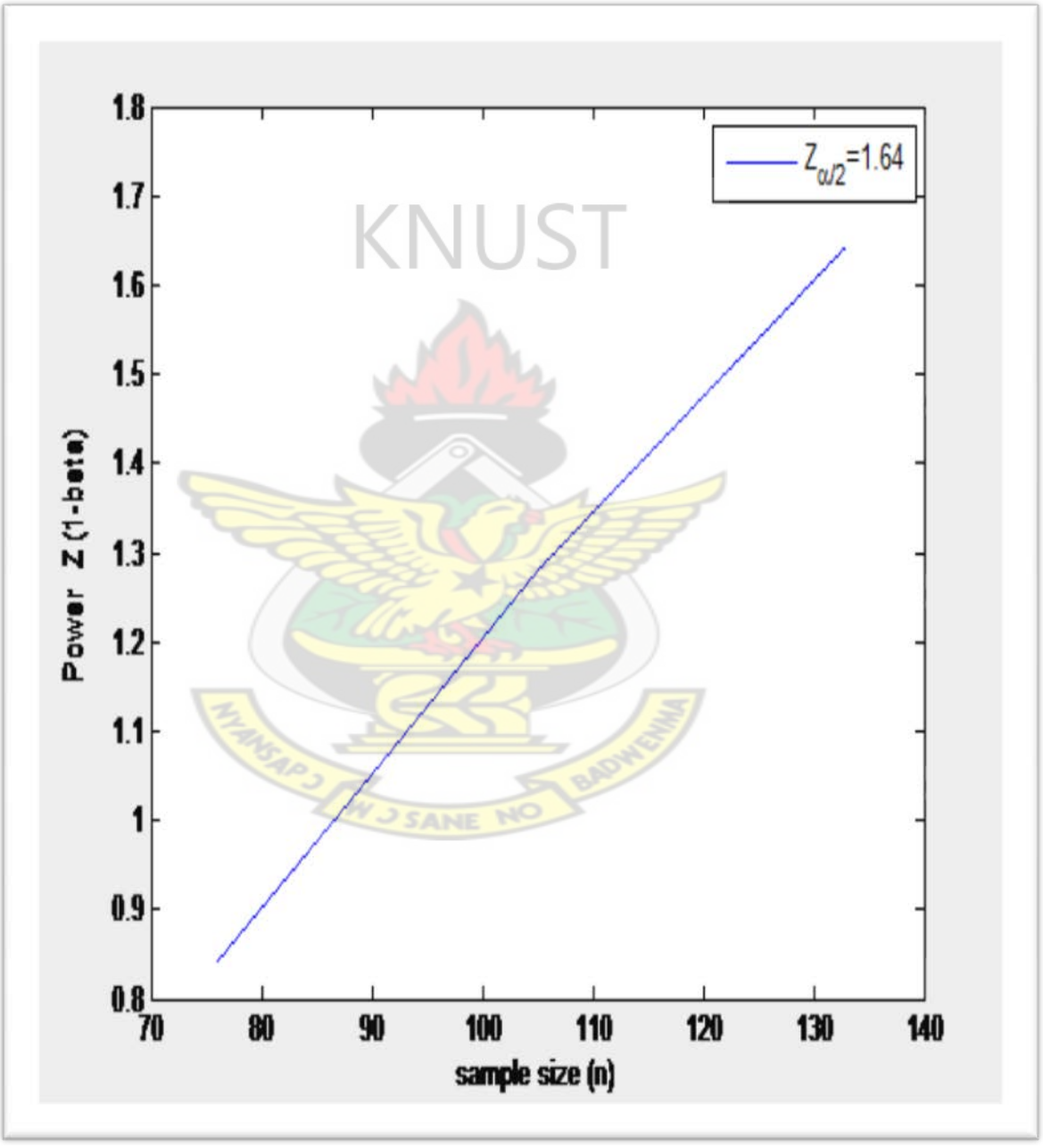
end

xlswrite('SampleSizeDetDiffSigma.xls',table)%Put the matrix table in excel and give it the nameSampleSizeDetDiffSigma.xls

APPENDIX_6

GRAPH OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN POPULATION PROPORTIONS AND USING 90% CONFIDENCE INTERVAL.

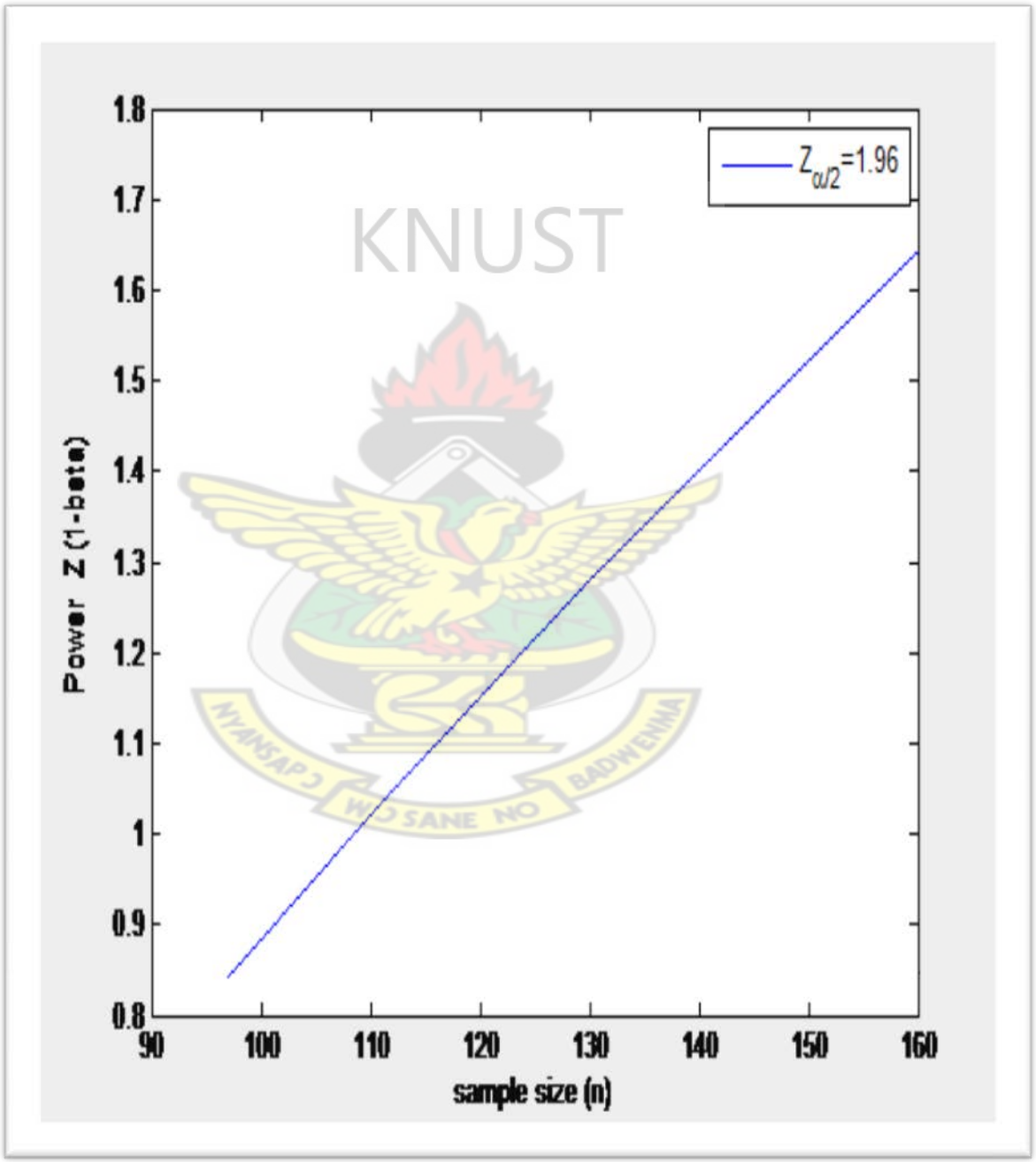
For $\hat{p}_1$ =0.6 and $\hat{p}_2$ =0.4



Graph of power against sample size (*n*), using difference in population proportions for α =1.64.

APPENDIX_7

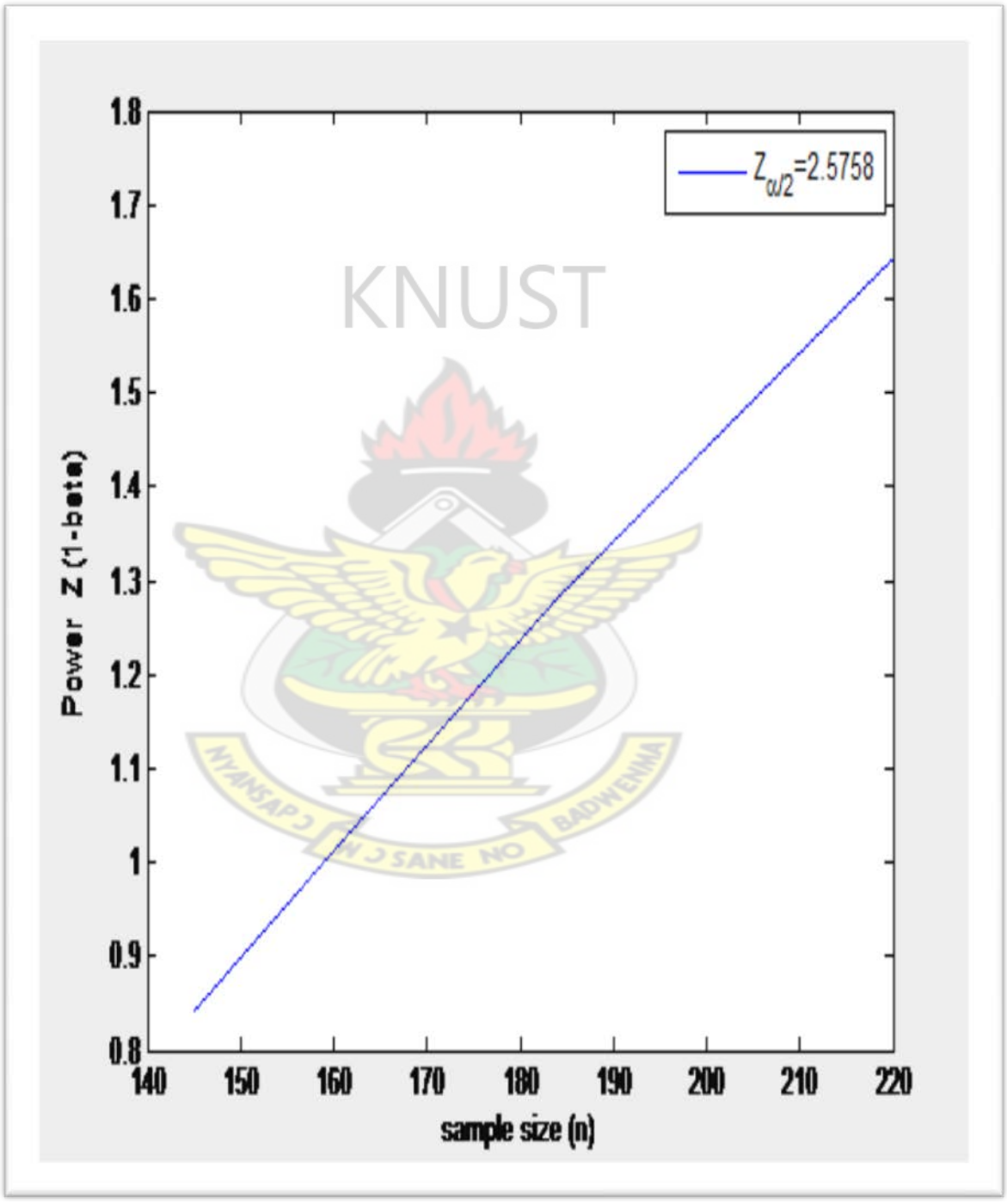
GRAPH OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN POPULATION PROPORTIONS USING 95% CONFIDENCE INTERVAL.



Graph of power against sample size (n), using difference in population proportions for α =1.96.

APPENDIX_8

GRAPH OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN POPULATION PROPORTIONS USING 99% CONFIDENCE INTERVAL.

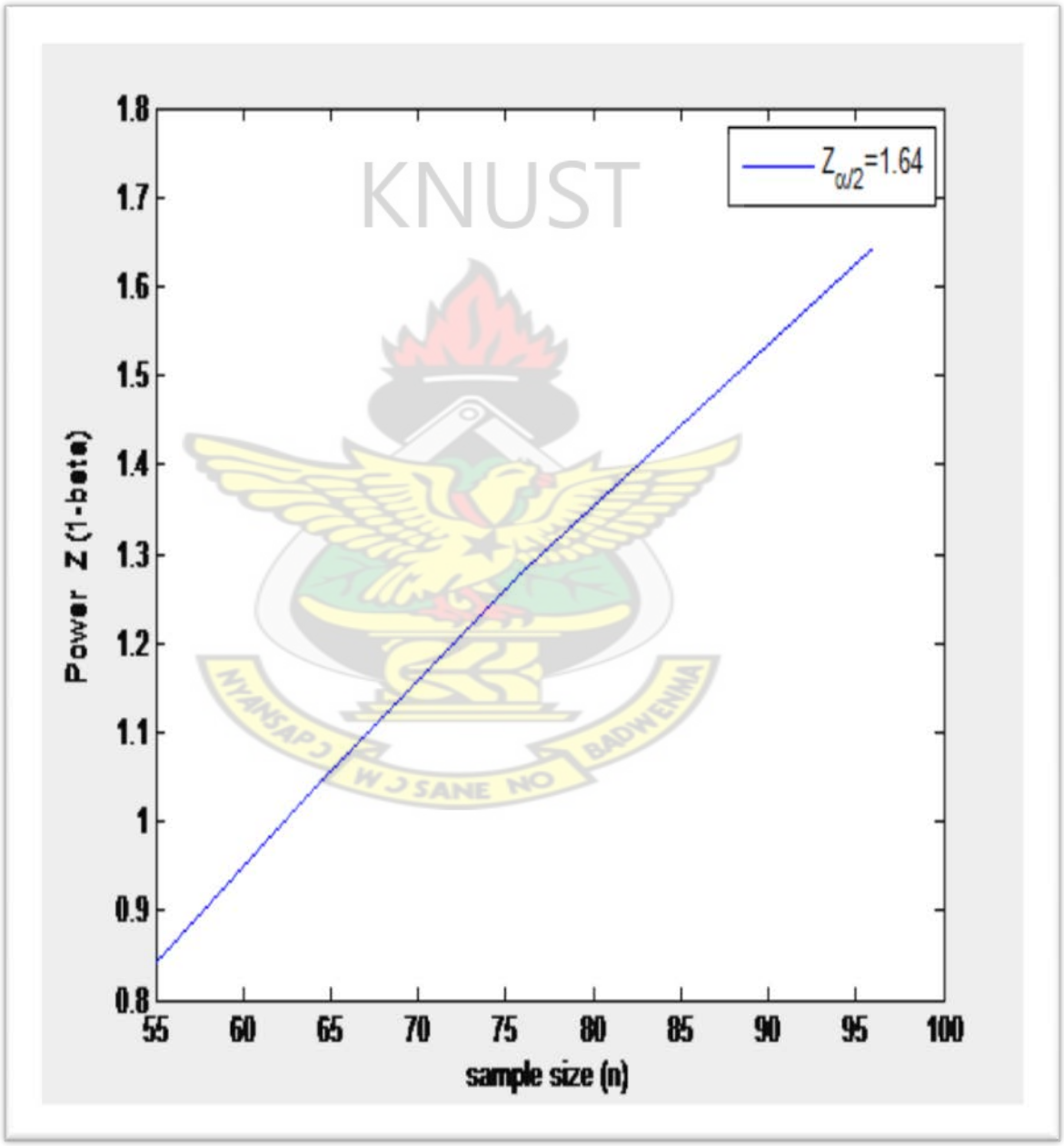


Graph of power against sample size (n), using difference in population proportions for α = 2.5758.

APPENDIX_9

GRAPH OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN POPULATION MEANS WITH COMMON STANDARD DEVIATION AND 90% CONFIDENDENCE INTERVAL.

For μ_1 =135, μ_2 =120 and σ =21

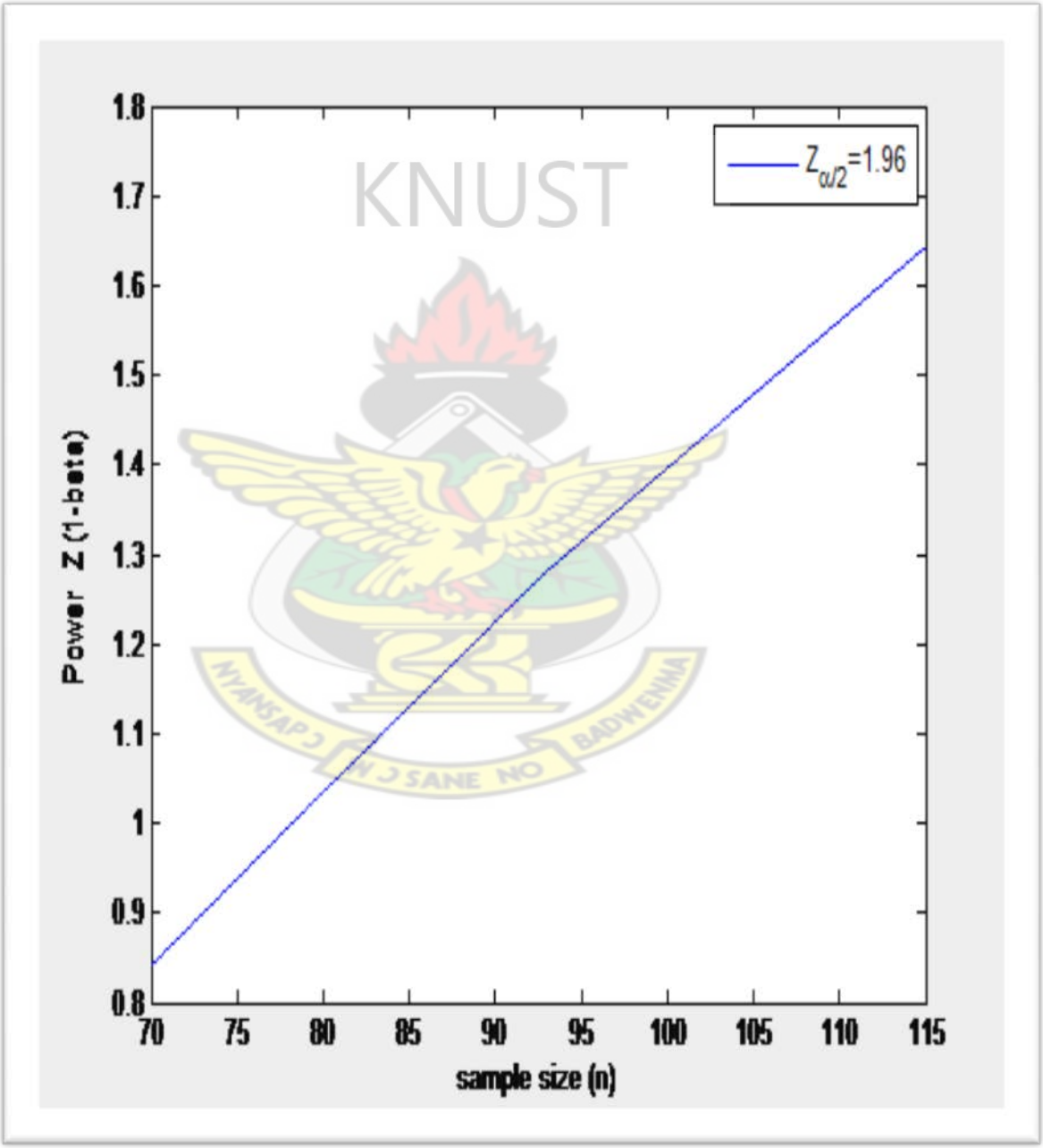


Graph of power against sample size (*n*), using difference in population means with common standard deviation for α =1.64.

APPENDIX_10

GRAPH OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN POPULATION MEANS WITH COMMON STANDARD DEVIATION AND 95% CONFIDENDENCE INTERVAL.

For μ_1=135, μ_2=120 and σ=21

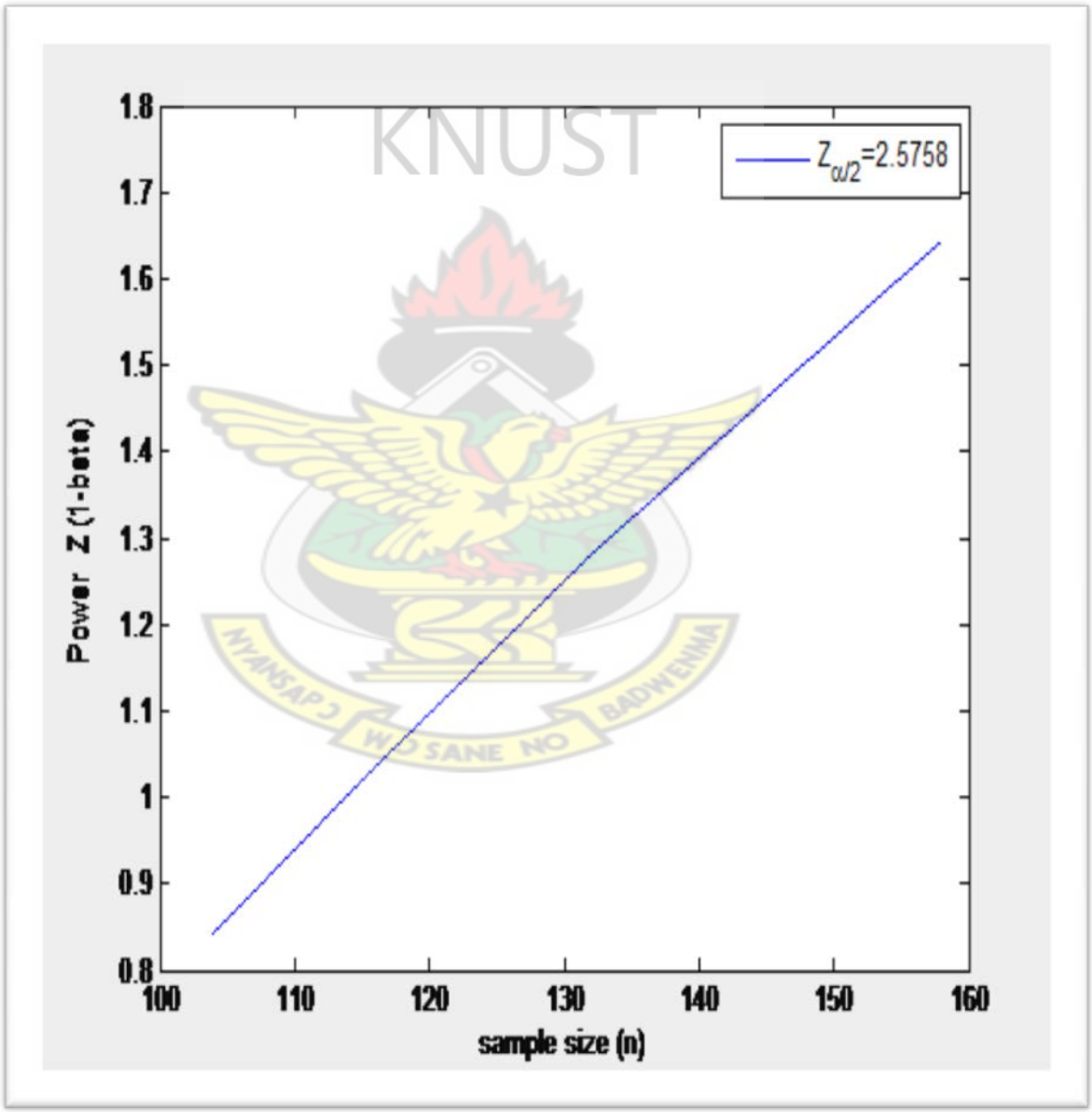


Graph of power against sample size (*n*), using difference in population means with common standard deviation for α=1.96.

APPENDIX_11

GRAPH OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN POPULATION MEANS WITH COMMON STANDARD DEVIATION AND 99% CONFIDENCE INTERVAL.

For μ_1=135, μ_2=120 and σ=21

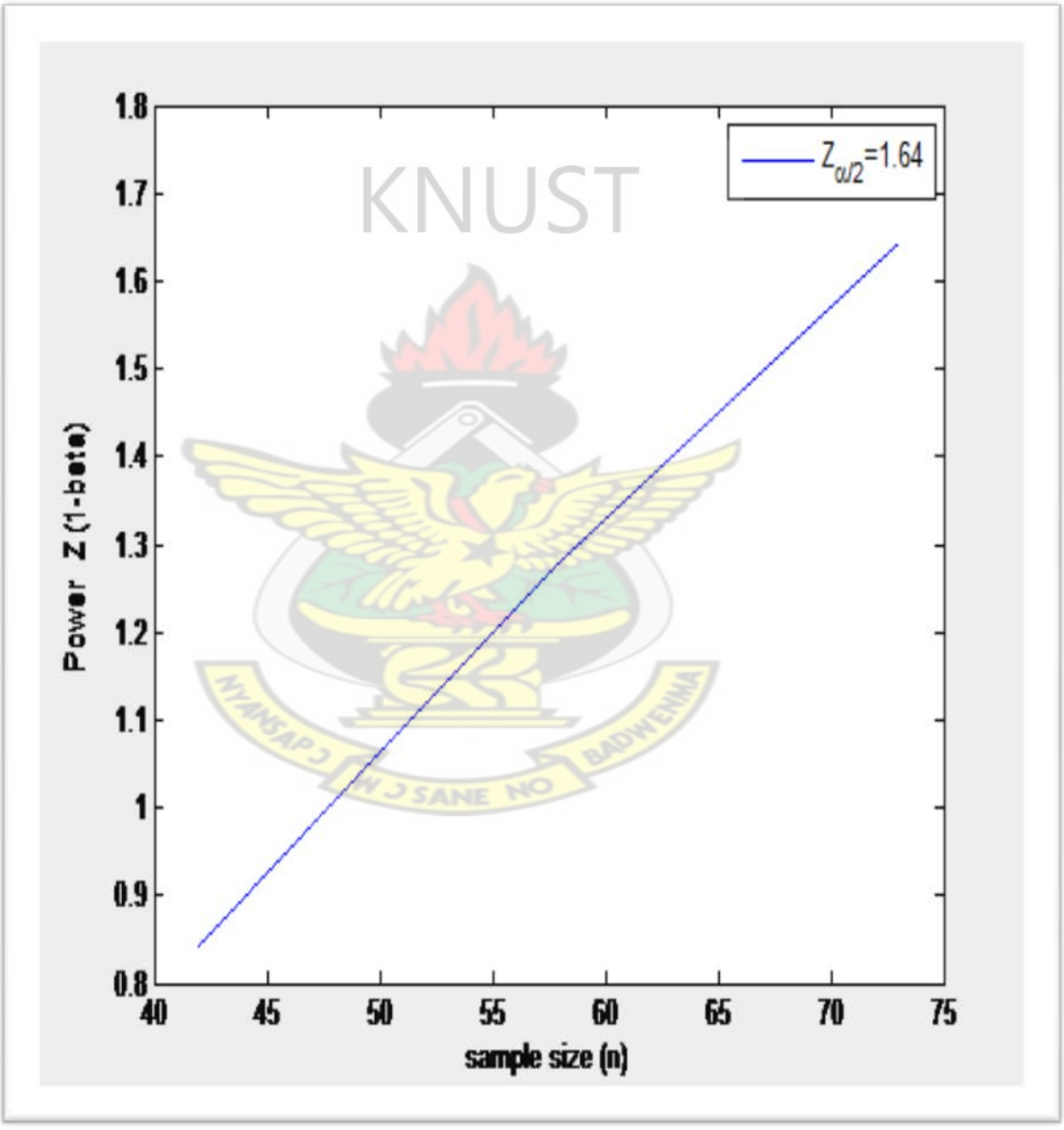


Graph of power against sample size (*n*), using difference in population means with common standard deviation for α=2.5758.

APPENDIX_12

GRAPHS OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN MEANS AND DIFFERENCE IN STANDARD DEVIATIONS WITH 90% CONFIDENT INTERVAL.

For μ_1=135, μ_2=120 and σ_1=32, σ_2=22

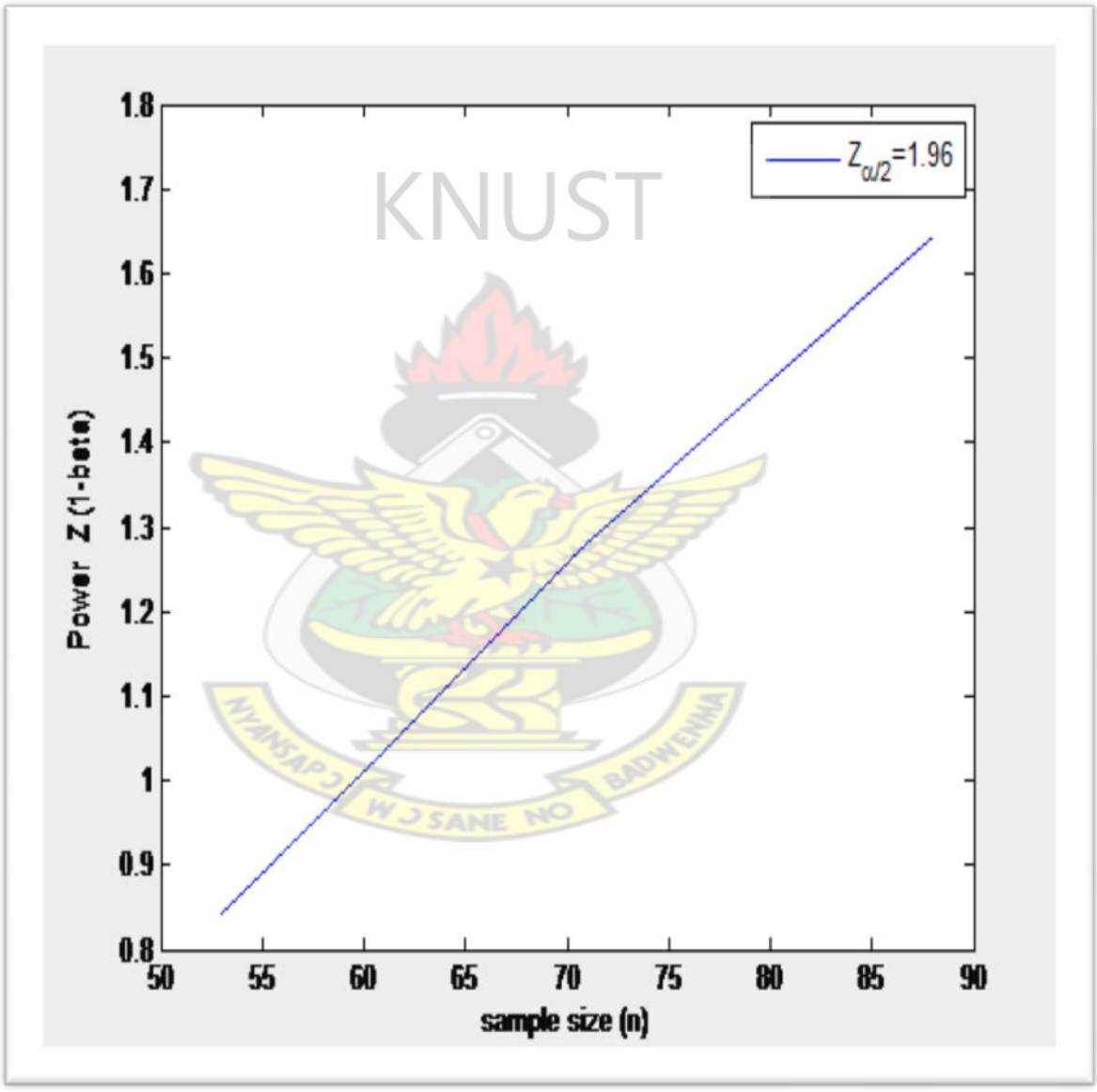


Graph of power against sample size (*n*), using difference in population means and different standard deviations for α =1.64.

APPENDIX_13

GRAPHS OF DETERMINING SAMPLE SIZES USING DIFFERENCE IN MEANS AND DIFFERENCE IN STANDARD DEVIATIONS WITH 95% CONFIDENT INTERVAL.

For μ_1=135, μ_2=120 and σ_1=32, σ_2=22



Graph of power against sample size (*n*), using difference in population means and different standard deviations for α =1.96.

APPENDIX_14

TABLE 4.3: SAMPLE SIZES DETERMINATION USING SINGLE PROPORTION

CI (%)	$Z_{(1-\alpha/2)}$	$\hat{p}_i$	E_i	N
90	1.64	0.1	0.025	388
95	1.96			554
99	2.57			956
90	1.64	0.5	0.03	784
95	1.96			1068
99	2.57			718
90	1.64	0.4	0.03	718
95	1.96			1025
99	2.57			1770
90	1.64	0.4	0.05	259
95	1.96			369
99	2.57			637

APPENDIX_15

TABLE: 4.4 SAMPLE SIZES DETERMINATION USING DIFFERENCE IN POPULATION PROPORTIONS

For $\hat{p}_1$ =0.6 and $\hat{p}_2$ =0.4

$Z_{(1-\beta)}$ / $Z_{\alpha/2}$	0.8416	1.0364	1.2816	1.6449
1.64	76	89	105	133
1.96	97	111	130	160
2.5758	145	162	184	220

For $\hat{p}_1$ =0.7 and $\hat{p}_2$ =0.3

$Z_{(1-\beta)}$ / $Z_{\alpha/2}$	0.8416	1.0364	1.2816	1.6449
1.64	19	21	25	31
1.96	24	27	31	38
2.5758	36	39	44	53

For $\hat{p}_1$ =0.5 and $\hat{p}_2$ =0.3

$Z_{(1-\beta)}$ / $Z_{\alpha/2}$	0.8416	1.0364	1.2816	1.6449
1.64	73	85	101	127
1.96	93	107	125	153
2.5758	139	155	177	211

APPENDIX_16

TABLE: 4.5 SAMPLE SIZE DETERMINATION USING MAXIMUM ERROR OF THE MEAN.

CI (%)	$Z_{(1-\alpha/2)}$	σ_i	E_i	N
90	1.64			4974
95	1.96	2.15	0.05	7104
99	2.57			12268
90	1.64	2.0	0.05	4304
95	1.96			6147
99	2.57			10616
90	1.64	2.0	0.03	11954
95	1.96			17074
99	2.57			29488
90	1.64	1.2	0.05	1550
95	1.96			2213
99	2.57			3822

APPENDIX_17

TABLE: 4.6 SAMPLE SIZES DETERMINATION USING DIFFERENCE IN POPULATION MEANS WITH COMMON STANDARD DEVIATION.

For μ_1=120, μ_2=132, σ=42

$Z_{(1-\beta)}$ / $Z_{\alpha/2}$	0.8416	1.0364	1.2816	1.6449
1.64	151	176	210	265
1.96	193	220	130	319
2.5758	287	320	184	437

For μ_1=62, μ_2=110, σ=42

$Z_{(1-\beta)}$ / $Z_{\alpha/2}$	0.8416	1.0364	1.2816	1.6449
1.64	10	11	14	17
1.96	13	14	130	20
2.5758	18	20	184	28

For μ_1=120, μ_2=132, σ=21

$Z_{(1-\beta)}$ / $Z_{\alpha/2}$	0.8416	1.0364	1.2816	1.6449
1.64	38	44	53	67
1.96	49	55	65	80
2.5758	72	80	92	110