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Meta-Analysis of Prevalence Rates of Anxiety Disorders in Kenya from 2000-2018

Research Report in Statistics, Number 43, 2019

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**Meta-Analysis of Prevalence Rates of Anxiety
Disorders in Kenya from 2000-2018**
Research Report in Statistics, Number 43, 2019

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Master Thesis

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Abstract

The goal of this project, was to use the available data from published documents to come up with a pooled effect estimate that can inform the Health policy and economic planning in Kenya using Meta-analysis of prevalence. Anxiety disorders have become a silent disease that is slowly taking away the skilled man power and the burdening the society at large as most of the times patients suffer in silent, and most of the times do not consider it as a disease. The study aimed at finding the pooled prevalence rate of Anxiety disorders in Kenya, investigate heterogeneity among studies, evaluate the degree of association of the substantive variables with the overall effect and finally check whether studies had publication bias. A total of 17 studies were included and the overall prevalence rate was 29% with 95% confidence interval of (15.3%, 44%) and after correcting the publication bias and excluding the outlier studies, the overall prevalence rate of Anxiety disorder in Kenya was 25.12% with 95% confidence intervals (19.32%, 31.40%). Substantial heterogeneity was evident and were explained by some moderator variables and the two outlier studies. It was also established that small studies with small study effects tend to be neglected and never get published while large studies with small effects have higher chances of getting published. We would recommend further research into the specific cases of Anxiety disorders and its impact on patients with lifetime diseases following a prospective study design.

Declaration and Approval

I the undersigned declare that this dissertation is my original work and to the best of my knowledge, it has not been submitted in support of an award of a degree in any other university or institution of learning.

Signature

Date

KORIR J SHARON

Reg No. I56/8543/2017

In my capacity as a supervisor of the candidate's dissertation, I certify that this dissertation has my approval for submission.

Signature

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Dedication

I dedicate this research work to my best friend and nephew, Leone K. Korir and to the African Mental Health Foundation.

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Nairobi, 2017.

1 Introduction

The aim of this thesis is to bring together the already available estimates to find an approximate combined effect that can inform decisions on Health policy and Economic planning in Kenya. This section explains in details what anxiety disorders are and the risk factors associated with the same.

1.1 Anxiety Disorders

Mental illness is a condition that affects one's functionality, behavior and perception towards life and situations. These include Depression (mood disorder), anxiety disorders, personality disorders, psychotic disorder, eating disorder and substance abuse disorder. These disorders are closely related as some share risk factors and one may lead to another.

According to WHO, the global burden of mental illnesses is on the rise and in the year 2014, approximately 450 million people were reported to be suffering from at least one mental disorder. On the other hand, access to health care services in low income countries has continued to be inadequate with an approximate gap of 85 percent as compared to the high income countries.

Anxiety is expected when faced with a problem or a situation that one is not so sure of how to go about, for example interviews, taking an exam, zip lining or even addressing new people. AD on the other hand is characterized by excessive and uncontrollable worry, fear and apprehension. Those who suffer from AD have an affected social life and are less productive since they are affected functionally.

Anxiety disorders, has remained as the most prevalent mental disorder that most of the times goes unnoticed until when it is too late and has affected the patient. It is mostly co-occurs with other depressive disorder and have common risk factors [Carlos et al., 2014]. The factors that co-exist for both disorders include individuals low self-esteem, genetics whereby there is a member in the family who has suffered before, female gender, females are at a higher risk as compared to male gender, number of years in education and an unstable or disturbed family environment [Carlos et al., 2014]. Anxiety disorder is also caused by misalignment of hormones and electric signals in the brain hence this risk factor only affects an individual and does not spread to their generation.

According to the National Institute of Mental Health together with The US department of Health services, there are five main types of anxiety disorders.

1. Generalized Anxiety disorder (GAD)- It is caused by excessive worry that gets out of control. The patient worries so much about normal routine things in life like work, children and in most cases one cannot tell what they are worried. This disorder is characterized by difficulty in concentrating or the mind goes blank, muscle tension, insomnia, irritability, shortness

of breath,feeling at the edge and restlessness. It takes at least six months to go away given the right treatment though in some cases it lasts even longer.Such people can hardly stay alone in an house.This condition can be severe and chronic in some instances and has a lifetime prevalence rate of approximately 6 percent[Nutt et.al.,2002]

2.Panic disorder-This is a recurrent fear that comes suddenly and reaches its peak within minutes.The attacks normally last for at least 45 minutes but may last longer in severe cases.The fear is normally triggered by a particular situation or thoughts.Panic attacks are strainious and very scary but not dangerous.This condition is characterized by sudden chest pains,thoughts of doom,trembling,shortness of breath,feeling out of control,sweating and increased blood pressure.The patients associate the attacks to a particular place or things hence they struggle to avoid since they are constantly worried about the next attack.Hence they end up developing Agoraphobia

3.Social anxiety disorder(Specific phobia and Agoraphobia) People affected by this order cannot take a negative comment and always think around humiliation and rejection.People with Specific phobias cannot face heights,certain animals,blood and others.**Agoraphobia** patients tend to avoid specific places because they thing escaping will be difficult.Such people can hardly stand in a line or crowd,use public transportation or even stay outside the house. They avoid contact with people and living becomes very difficult.In kids is known as **Selective mutism**,these kids cannot speak in some social situations despite having the right skills.They only speak around people they are used to.

4.Obsessive-Compulsive disorder-Characterized by recurrent unwanted thoughts and repetitive behaviors.This disorder is characterized by actions like repeatedly counting things,checking if the door is locked many times,washing and rubbing hands,hoarding unimportant items and constantly seeking re-assurance.

5.Post Traumatic stress Disorder-This happens to people who have undergone a traumatizing experience like separation or grieve and never make it to overcome the experience.**Separation disorder** is a special type of PTSD which specifically affects children.These children have a constant fear and nightmares of being separated to the people they are attached to.

1.1.1 Risk factors for Anxiety disorders

A risk factor is is a variable that precedes an outcome measure.The above mentioned disorders share some risk factors like history of anxiety in the family,exposure to negative and stressful event or environment ,behavioral inhibition in childhood.Sometimes suffering from AD might be a sign of an underlying medical problem for example Heart Arrhythmia or Thyroid problems.

A recent meta-analysis has shown that anxiety disorders follow a familial aggregation,where this are the common set of behaviours and disorders within a family that is

genetically related or due to the environment. Results from the Meta-analysis showed that, Anxiety disorders such as GAD, panic disorders, phobias and OCD follow a substantial familial aggregation.

A significant association was obtained between panic disorder in pro-bands and their first degree relatives [Michael et.al.,2007].

1.1.2 Cormobidity of Anxiety Disorders

Cormobidity is generally defined as the existence of one or more conditions co-occurring with a primary condition. Majority of the people suffering from and Anxiety disorder meets the criteria for more than one anxiety disorder. The study conducted by [Michael et.al.,2007] shows that there is a positive association between lifetime occurrences of all the pairs of Anxiety disorder. Strong positive association between GAD and panic disorders and panic disorder with Agoraphobia. The odds for developing GAD is 12.3 times higher and 11.9 times higher for developing Agoraphobia for people with panic disorder than for people who do not suffer from panic disorder. However, the association between PTSD with other Anxiety disorders were low, the odds between 2.8 and 4.2.

Anxiety disorders are also cormobid with other mental disorders especially Affective disorders substance use disorder and Somatoform disorders [Michael et.al.,2007]. However more evidence on the exact odds of association are still not estimated since the information is still sparse.

Global prevalence of anxiety disorders, by age and sex (%)

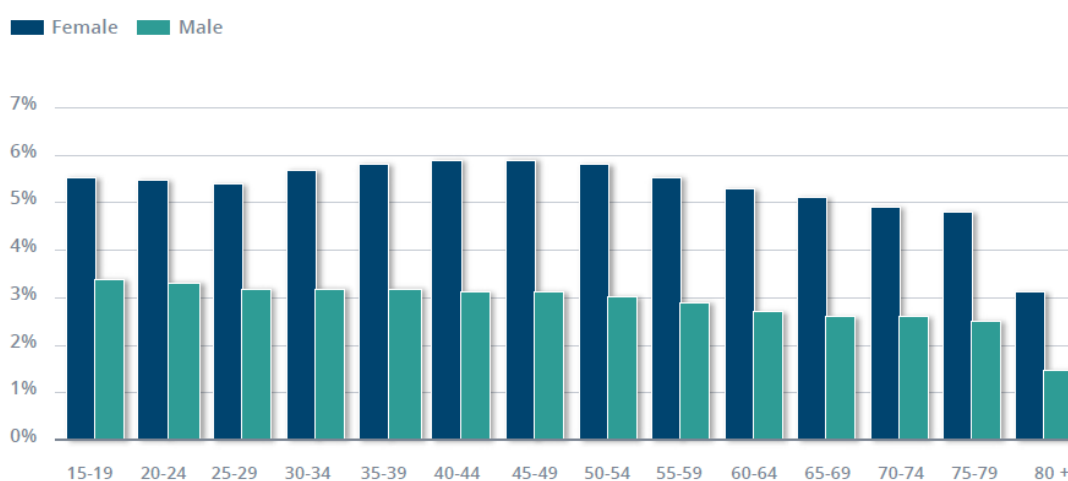


Figure 1. Global Burden of disease,2015
[Global Burden of Disease,2015]

Basing on the results obtained from the Global Burden of Disease,2015,the World Health organization concludes that Anxiety Disorders affects all the people across all the age groups but females are at a higher risk as compared to males.

1.2 Objectives

1.2.1 Main Objective

To determine the pooled prevalence rate of Anxiety disorders in Kenya.

1.2.2 Specific Objectives

- To investigate heterogeneity across studies included in the meta-analysis.
- To test whether the moderator variables have an impact towards the summary effect
- To test whether the publications included in the study were biased.

1.3 Statement of Problem

Generally, mental health has not been given the attentions it deserves especially in developing countries where it is neglected and under-resourced [Ndeti et al., 2011]. AD was rated by WHO in 2015 as the sixth largest contributor to non-fatal health loss globally, while it creeps in so silently and in most cases goes unnoticed until it's too late. It is estimated that 1 out of 20 people in primary health care receive proper treatment and therapies. People with AD face discrimination, under treatment and have the lowest employment rates since they are not productive causing an economic burden to the specific families and the country. People with AD are less productive as compared to other mental disorders like depression, this is because disorders are associated with a lower average level of disability (WHO, 2015). A particular trend cannot be drawn for Kenya to evaluate itself on how far anxiety disorder has been dealt with in the country. Very few studies have been conducted and in few areas hence might not be used to draw a trend. The Global Burden of Disease (GBD) project provides a strong basis for evaluating the comparative impact of disease based on composite measures of disease occurrence (prevalence and incidence rates), mortality and disability. The study conducted in 1990 on Global burden of disease demonstrated that mental disorders, majorly depression and anxiety disorders, made a substantial contribution to the global burden [Murray et al.].

1.4 Justification of the Study

Provision of estimates of the population affected by a medical condition is very essential in informing the Health policy, economic planning and performance evaluation in a country. The Kenya Mental Health policy 2015-2030 [Health policy], which basically aims at securing Mental Health systems in Kenya, indicates that its main challenge is the inadequate information and data on the prevalence of Mental disorders. Thus this study aims to solve the said issue by bringing together what is available to come up with an estimate that can inform critical decisions. Anxiety disorders have been proved to have a strong positive correlation with suicidal thoughts. There have been increased cases of reported suicides and killings in Kenya since people cannot face the future. Over 70 percent of people with anxiety attempt suicide during their lifetime [Nepon et al, 2010]

There is a lot of economic burden caused by patients affected with anxiety disorders since they are not productive and the cost of treatment. According to WHO the global burden caused by AD was at Here in Kenya only 0.5 percent of health budget is allocated to mental health. It is estimated that Kenya has only 500 psychiatrists, hence mental health is under-resourced. Only a small percentage of patients at primary care receive full treatment, some of these conditions go unnoticed until when it is too late. Women are at a dire risk of anxiety and even depression during pregnancy and even after birth, this poses a risk to the life of the infants which leads to increased rate of infant mortality (Husain et al, 2016)

2 Literature review

2.0.1 Preliminaries

In this section, we will discuss the results and information on Anxiety disorders obtained from publications made by other scholars and even companies. Different approaches used to arrive at the solutions on Anxiety disorders and also the existing gaps recommended for future areas of focus.

2.0.2 Systematic Review

In the year 2012, a meta-regression and systematic review was conducted in the to determine the global prevalence rate of Anxiety disorders and the results were approximated to range between 0.9% and 28.3% which had a slight difference from the previous year results whose range was 2.4% -29.8% [Baxter et.al.,2012]. A total of 87 studies, that had been published between 1980 and 2009 were included in the study and that was a representation of 44 countries. It was evident that the moderators like gender, age, culture, economic status, conflict and urbanity were responsible for the great variability observed. The period of time that the prevalence rate was recorded, the number of disorders and the instrument used for diagnosis through the multivariate model explained the additional 13% between-study variance. The study was able to explain much of the variability though the authors insisted on consideration of cultural differences in relation to survey instruments for ,more specific results for Anxiety disorders. The estimates for specific anxiety disorders were not captured [Baxter et.al.,2012].

A study carried out in 2013 among adult patients in an outpatient clinic in Nairobi-Kenya, 56% of the patients experienced co-morbidity, with 19% of the patients experiencing both mood disorder and Anxiety disorder. Approximately 29.7% of the patients experienced more than one current mental disorders while one in every set of ten patients was at a risk of committing suicide. The most prevalent mental disorders reported were Affective disorder, Anxiety, Somatoform and depressive disorders. There was a positive correlation between Gastritis and mental disorder [Aillon et.al.,2013]. It was noted that other socio-demographic factors like level of education ,gender, employment and marital status highly affected the development patterns of any mental disorder. The study highlighted the importance of proper therapeutic methods to differentiating the specific mental disorders, association with other diseases, co-morbidity and the risks associated to such

illnesses[Aillon et.al.,2013].

A cross-sectional study carried out at the Premier Psychiatric Hospital in Kenya-Mathari in the year 2013 ,the chi-square test of association prevalence rates of mental disorders in men as compared to women.Those involved in the study were patients who had been there for four years hence consented to participate in the study,which only approximately 14.5% were heads of households,this meant that around 85% of the data set depended on their families and relatives[Ndetei et.al,2008].Anxiety disorder was rated as the fifth most prevalent after Schizophrenia,Bipolar I,substance use disorder and Major depressive disorder with the prevalence rates of 51%,42.3%,34.4% and 24.6% respectively[Ndetei et.al,2008].The specific Anxiety disorders were very common with Post Traumatic disorder reported at 33.3% while 24.6% of the patients were under treatment for the disorder that they had been diagnosed with previously.14.7% of those suffering from depressive disorder had attempted suicide before.Pearson's 2-tailed test on correlation had showed significant co-morbidity of mental disorders.The authors however insisted that Anxiety Disorders were very hard to diagnose hence hard to manage as well[Ndetei et.al,2008].

The study carried out in Kilifi- Kenya in 2013 mainly focused on accessing whether parenting behaviours and the parents mental experiences were possible risk factors for developing any mental disorders in children[Kariuki et.al,2017].Mental depressive disorder in children has been proofed to be caused by negative parenting behaviour and major depressive disorder in parents[Khasakhala et.al,2013].Children who are exposed to these risk factors have the odds ratio of 2.41 with a 95% confidence intervals of 1.20 and 4.87.[Khasakhala et.al,2013].This implies that children exposed to those risk factors are 2.4 times more likely to develop any anxiety disorder as compared to the children who are not exposed.Children also experience behavioural and emotional problems basing on the risk factors they are exposed to[Kariuki et.al,2017].A study in Kilifi showed that children between the age of 1 and 6 had high prevalence of psychological disorders after exposures to risk factors that are preventable.The following risk ratios were recorded for the following risk factors;Children who ate cassava 5.68(3.22,10.03) ,prenatal complications 4.34(3.21,5.81),seizure 2.90(2.24,3.77) and house status 0.11(0.08,0.14)[Kariuki et.al,2017].The prevalence of anxiety disorder was at 13%.[Kariuki et.al,2017].

The proportion of the global population with anxiety disorders in 2015 is estimated to be 3.6%. As with depression, anxiety disorders are more common among females than males (4.6% compared to 2.6% at the global level). According to the WHO,2017,the Africa region contributes 10% of the global prevalence rate of AD with approximately 25 million people suffering from the same.The Prevalence rates did not vary substantially between age groups, however a low trend was observed among older age groups.The total estimated number of people living with anxiety disorders in the world is 264 million as at 2015

marking an upward trend of 14.9% from 2005.

In the year 2016, a systematic review and meta-analysis was carried out to pool the prevalence rate for chronic pain in the general population [Mansfield et al., 2016]. The authors assumed the studies did not share a common effect size hence considered a random effects model to pool results from publications made from the year 1990. The prevalence rates from the final 24 studies compared were a real representative of the population and the studies with high risk of biased measurements may be as a result of extrapolation were excluded. This reduced the level of heterogeneity from 98% to 95%. The authors considered the double arcine transformation of the prevalence rates to improve their statistical properties. This study however considered risk of bias, geographical location and data collection method used as the main sources of variation among the prevalence rates of pain [Mansfield et al., 2016].

A study conducted by a PHD student in 2018, Kathleen in Australia to study the time trends in prevalence of global mental disorders was achieved using a standard diagnostic tool administered to the parents of the children and the youths involved [?]. The study compared prevalence across two time points with an interval of 15 years 1998, 2013 and 2014. The prevalence rates of mental disorders among the youths and children was observed to have had a very slight difference even with time. In 1998, the prevalence rate was 12.5% with 95% confidence intervals (11.4% - 13.7%) while in 2013 to 2014 the prevalence rate was at 11.1% with 95% confidence intervals (10.1% - 12.2%). This study's strength was the power of its samples, the 3597 participants in 1998 and 5659 in 2013-2014. However the study's weakness is relying on the parents views whose judgement might have reported low levels of prevalence than it actually was.

The previous studies have shown the existence of the mental disorders and the prevalence of Anxiety disorders across all ages around the globe. The studies that have used meta-regression as shown the importance and what achievement this way of pooling effect sizes can give, however this has never happened in Kenya, hence this study is in place to fill the gap. The meta-regression carried out before considered a double arcine transformation whereas this study will consider logistic transformation of proportions. The global estimate of prevalence rates across 44 did not put into consideration the cultural differences between countries which might have caused a great variability in the results. The question behind the reported global prevalence rate is whether the estimate given applies to a specific country since there is a probability of 0.6 that a country was not selected into the sample. The studies on prevalence of Anxiety disorders in Kenya so far by other researchers have been carried out in different parts in the country involving different age groups and different set ups. This study therefore seeks to bring together this estimates to establish whether the prevalence rates among children in Western Kenya and that in the

coastal region can be brought in to a conclusion and know our position on Anxiety as a country. This will make it more easy in planning at the National level on Health policy.

3 Methodology

3.1 Introduction

This chapter entails the study selection process, and all the statistical procedures, mainly the test statistics that were estimated in the study and the software used.

3.2 Data Extraction and Analysis

Data was collected from papers published between the year 2000 and 2018 following DECiMal [Pedder et al., 2016] guidelines. Substantive factors such as age categories, gender, study design and the coverage were captured which were in this case the moderator variables. Records were obtained from Pubmed and Google scholar databases with meSH words being *Anxiety disorder(s), Kenya, Prevalence* with sub-heading as *Epidemiology*, full texts were obtained with a specified 18-year timeline 2000-2018. The data was entered in Excel and later imported to R-statistical software for analysis and tests. This study assumes a random effects model and that prevalence follows a binomial distribution.

3.2.1 Study selection process

The 48 studies had captured the meSH words hence qualified to the selection. There was a single study that had been published on both databases. Full texts of the documents were obtained and reviewed to record the details included in each study, including the author, year, the setting or environment in which the study was carried out, the age group and gender included, the study design, the population and the Region in which it was carried out. During the review, 31 studies were excluded since it did not contain the exact information that was required for this study for example some only brought out the risk factors of anxiety disorders without necessarily reporting its frequency while some reported a general prevalence rates including other mental disorders hence this could not be selected as the exact prevalence of Anxiety disorders could not be singled out.

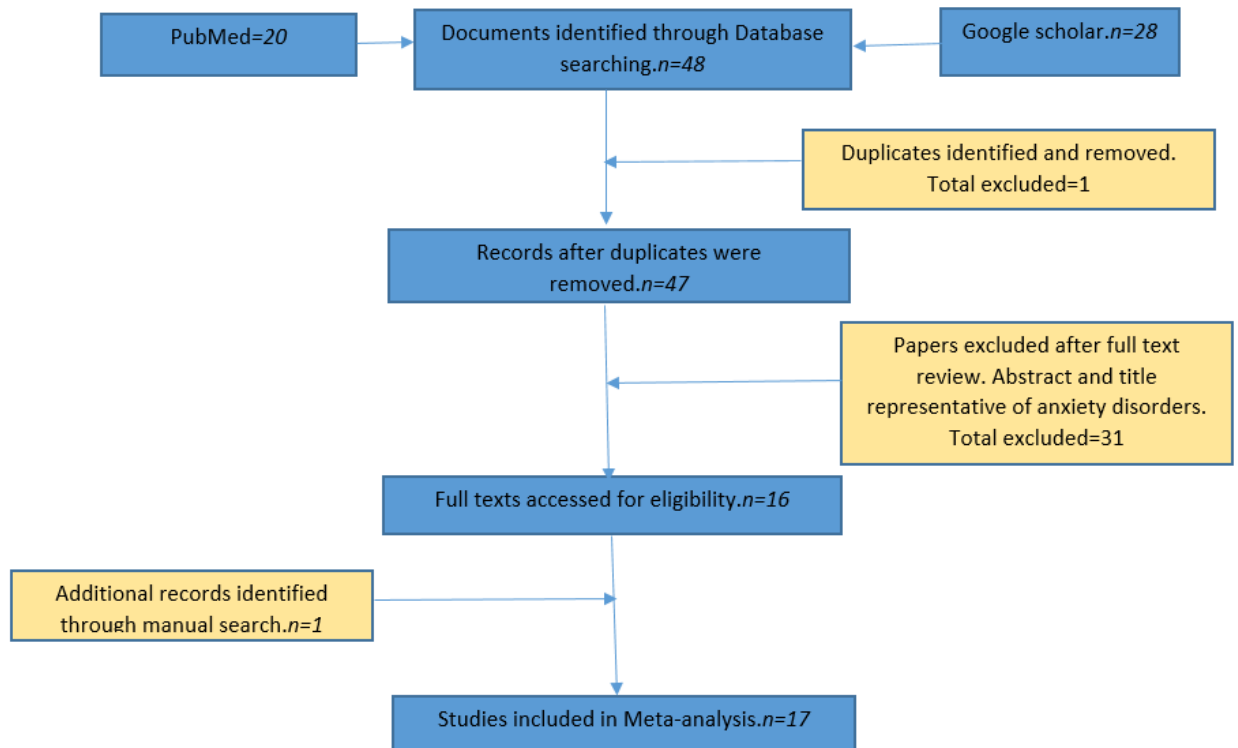


Figure 2. Prisma flow diagram

3.3 Meta-analysis

Meta-analysis, is a set of statistical techniques used to find a pooled estimate of an effect across several studies. The word "Meta" was derived from Greek which basically means, "after", "along" or "later". This method of data synthesis requires that there are more than one studies which have estimated the effect of a treatment/intervention or risk factor and the studies must have been carried out in closely similar settings so that we are certain of combining the data comfortably. It is also necessary to be able to find both the estimates of the effects and also their standard errors. Meta-analysis is important in obtaining pooled estimate of an effect and confidence intervals, testing whether treatments and the risk factors are statistically significant and to test heterogeneity/similarity of the outcome across studies. [?]. The level of precision differs for all the studies conducted depending on the sample size and the study design used. This is the reason we compute weighted mean in Meta-analysis instead of computing the simple mean for the effect sizes.

There are two models we can assume in Meta-analysis, Fixed effects and Random effects model. In fixed effects model is based on the assumption that there is a common effect size across all the studies. Weights are assigned based on the size of the study whereby, the study with large observations are assigned more weights while studies with smaller observations are assigned lesser weights or are ignored. However, in random effects model, we assume that the true effect could vary from one study to another due to such parameters as age, weight, marital status e.t.c. [Borenstein et.al, 2007] This is known as **the assumption of exchangeability** [Schwarzer et.al, 2015]. According to [Borenstein et.al, 2007], in random effects model, weights are assigned in a balanced so that do study seem to dominate over the other. This study assumed a random effect model.

3.4 Meta-analysis of prevalence

Meta-analysis is very useful in pooling effect sizes basing on different measures such as relative risk, odds ratios, Risk difference/weighted/standardized mean difference and frequency of diseases (incidence rates and prevalence rates) [Barendregt et.al, 2013]. This study mainly focuses on pooling prevalence rates. Prevalence is a variable that is defined as the number of cases of a given condition or a disease divided by the number of the population, hence its specific characteristics. Prevalence is the number of existing cases of a disease at a given time, it depends on both incidence and the duration of the particular disease [Woodward M., 1999]. Incidence is the number of new cases at a given point and time.

$$P = ID \quad (1)$$

Is the relationship between, prevalence, incidence and time or duration. Prevalence is a variable with two specific characteristics; prevalence is always between 0 and 1, the sum of all categories is equal to one. It is assumed that prevalence follows a binomial distribution, which is the number of successes in a sample, hence in order to calculate the individual study weights the variance is obtained as follows;

$$var(p) = \frac{p(1-p)}{N} \quad (2)$$

Where; P is the proportion and N is the population size.

The individual study weights are then calculated as below;

$$P = \frac{\sum_i \frac{p_i}{var(p_i)}}{\sum_i \frac{1}{var(p_i)}} \quad (3)$$

P is the pooled prevalence or the overall estimate of prevalence which is the subject of the study.

In order to obtain 95% Confidence interval where the overall estimates lies, standard error is calculated as below;

$$SE(P) = \sqrt{\sum_i \frac{1}{var(p_i)}} \quad (4)$$

Confidence intervals will be given as;

$$CI = P \pm Z_{\alpha/2} * SE(P) \quad (5)$$

$Z_{\alpha/2}$ is the appropriate factor from the standard normal table distribution for the chosen level of significance. In this case this value was 1.96 due to 95% confidence interval.

3.4.1 Transformations

This is the process in which the prevalence rates are undergo a conversion to improve their statistical properties which helps to stabilize the variance. The prevalence is transformed to a variable that is not constrained to 0..1 range ensuring it follows an approximately normally distribution. This process is important because when the value of proportions approach 0..1 range, the equation for confidence interval does not preclude confidence limits outside the 0..1 range and when the proportion becomes too small or big the variance of the study is squeezed towards 0 hence the study gets an undue weight at the extreme of 0..1 range [Barendregt et.al, 2013]. Most studies argue that double arcine transformation gives a better result as compared to logit transformation since the former does not succeed in stabilizing the variance. This study considered using both logit transformation and double arcsine transformation and see whether the summary proportions would differ. The meta-analysis is carried out using the converted proportions using the Dersimonian Laird method (Inverse variance method). Finally, the pooled proportion is transformed back together with its confidence interval for easy interpretation.

Logit transformation

The logit transformation is given by;

$$l = \ln\left(\frac{p}{1-p}\right) \quad (6)$$

Variance;

$$var(l) = \frac{1}{Np} + \frac{1}{N(1-p)} \quad (7)$$

Inverse variance weight;

$$w_i = \frac{1}{se^2} = np(1-p) \quad (8)$$

To obtain the final proportion, the below equation is solved for P;

$$P = \frac{\exp(l)}{\exp(l) + 1} \quad (9)$$

3.4.2 Double Arcsine transformation

The estimate is obtained as follows;

$$ES_t = \frac{1}{2}(\sin^{-1}\sqrt{\frac{k}{n+1}} + \sin^{-1}\sqrt{\frac{k+1}{n+1}}) \quad (10)$$

Variance;

$$Var_t = \frac{1}{4n+2} \quad (11)$$

Back transformation;

$$P = \frac{1}{2}[1 - \text{sgn}(\text{cost})\sqrt{1 + (\text{sint} + \frac{\text{sint} - \frac{1}{\text{sint}}}{n'})^2}] \quad (12)$$

Where n' is the harmonic mean given by;

$$n' = m(\sum_i^m n_i^{-1})^{-1} \quad (13)$$

3.4.3 Random Effects Model

$$T_i = \theta_i + e_i = \mu + \varepsilon_i + e_i \quad (14)$$

Where;

T_i -observed effect

θ_i -true effect

e_i -within study error

μ -mean of all true effects

ε_i -between study error

But;

$$\theta_i = \mu_i + \varepsilon_i$$

In order to find between studies variance, τ^2 we have to find the total variance then isolate the within-studies variance. The **Dersimonian-Laird method** was used [Dersimonian, 1986] but since the method is said to give false results sometimes (Int Hout et al., 2014) especially when the number of studies included in Meta-analysis is small and shows substantial heterogeneity [Hartung, 1999]. Thus the **The Hartung-Knapp-Sidik-Jonkoman method** (HKSJ) was applied for sensitivity analysis since it has been proofed to outperform the Dersimonian-Laird method [Int Hout et al., 2014]).

$$Q = \sum_{i=1}^k W_i (T_i - \bar{T})^2 \quad (15)$$

Q is the total variance, W_i is the inverse of variance of each study, T_i is the sum of squared deviations from specific studies and \bar{T} is the combined mean.

Alternatively;

$$Q = \sum_{i=1}^k W_i T_i^2 - \frac{(\sum_{i=1}^k W_i T_i)^2}{\sum_{i=1}^k W_i} \quad (16)$$

The expected value of Q is the degrees of freedom which is obtained by subtracting one from the total number of studies included, N.

$$df = N - 1 \quad (17)$$

$$T^2 = \begin{cases} \frac{Q-df}{C}, & \text{if } Q = df \\ 0, & \text{if } Q \leq df \end{cases} \quad (18)$$

Where C is the scaling factor obtained as follows;

$$C = \sum W_i - \frac{\sum W_i^2}{W_i} \quad (19)$$

Assigning weights to specific studies and obtaining the weighted mean, \bar{T}^* .

Assigning weights to specific studies and obtaining the weighted mean, \bar{T}^* of within-study variance for the i 'th study and the between studies variance, τ^2

Specific weight is obtained as follows;

$$W_i^* = \frac{1}{V_i^*} \quad (20)$$

V_i^* , is the sum The weighted mean is then computed as the sum of products of specific effect size multiplied by weight divided by the sum of weights as shown below.

$$\bar{T}^* = \frac{\sum_{i=1}^k W_i^* T_i}{\sum_{i=1}^k W_i^*} \quad (21)$$

In order to find the standard error of the weighted mean, we first compute the variance of the combined effect which is the reciprocal of sum of weights.

$$V^* = \frac{1}{\sum_{i=1}^k W_i^*} \quad (22)$$

The standard error is given by the square root of variance;

$$SE(\bar{T}^*) = \sqrt{V^*} \quad (23)$$

The 95% confidence interval is obtained as follows;

$$UCI = \bar{T}_i^* + 1.96 * SE(\bar{T}_i^*) \quad (24)$$

$$LCI = \bar{T}_i^* - 1.96 * SE(\bar{T}_i^*) \quad (25)$$

The Z value, is very important in computing the p-value and is computed as follows;

$$z^* = \frac{\bar{T}_i^*}{SE(\bar{T}_i^*)} \quad (26)$$

The one tailed p-value is obtained as follows;

$$p^* = 1 - \phi(|z^*|) \quad (27)$$

Considering a two tailed p-value ,we have;

$$p^* = 2[1 - \phi(|z^*|)] \quad (28)$$

3.5 Heterogeneity Measures

Heterogeneity is the extent to which effect sizes vary within a Meta-analysis .It is a large variation or inconsistency observed in the study effects across studies.It is very important to check because high heterogeneity could be as a result of two or more subgroups of studies included in the data which have a different true effect.This information is very critical for research since it might allow us to find certain interventions for which an higher or lower.Extremely high heterogeneity means there is no real true effect meaning out Meta-Analysis can be considered meaningless hence the pooled effect cannot be reported.But researches can choose to consider random effects model which allows for heterogeneity.

There are three types of heterogeneity [Rucker et.al.,2008],**Clinical heterogeneity** caused by clinical factors like including very old or very young people in studies,**Statistical heterogeneity** which arises due to issues like sample size determination and others such as the study design chosen for a particular study.This study tested the same using the following methods,where;

k —denotes individual studies

K =number of studies included in meta-analysis

$\hat{\theta}_k$ -the estimated effect of k with variance $\frac{2}{k}$

w_k -is the specific study weights in other words is the inverse of individual variances.

Cochran's Q-statistic

This is the difference between observed effect sizes and fixed effect model estimate the effect sizes which is then squared, weighted and summed.

$$Q = \sum_{k=1}^K w_k \left(\hat{\sigma}_k - \frac{\sum_{k=1}^K w_k \hat{\sigma}_k}{\sum_{k=1}^K w_k} \right)^2 \quad (29)$$

This is the percentage of variability in the effect sizes which is not caused by sampling error, it is derived from the Cochran's statistic [Higgins Thompson, 2002].

Higgins's Thompson's I^2

This is the percentage of variability in the effect sizes which is not caused by sampling error, it is derived from the Cochran's statistic (Higgins Thompson, 2002).

$$I^2 = \text{Max}\left(0, \frac{Q - (K - 1)}{Q}\right) \quad (30)$$

The Q statistic increases with increase in the number of studies and the level of precision. It highly depends on the size of meta-analysis hence its statistical power, hence we cannot rely on it to making conclusions on heterogeneity. I^2 in the other hand is not sensitive to changes in the number of studies included in meta-analysis hence is mostly used in psychological and other medical researches. When $I^2 = 25\%$, we report low heterogeneity, $I^2 = 50\%$, moderate heterogeneity and when $I^2 = 75\%$ we say we have substantial heterogeneity. We do not make conclusions basing on this measure as it is highly dependent on the level of precision. τ^2 is insensitive to both precision and number of studies included. Confidence intervals however help solve all the shortcomings as they provide a range for which the effects of studies are expected to fall in future.

3.6 Diagnostic tests

These are graphs of individual studies included in Meta-analysis and influential cases are studies which show extreme values in the graphs. These are tests that were carried out on the studies meta-analysed to detect the extent to which the caused heterogeneity and the amount of influence on the pooled effect size obtained or whether a certain study was responsible for the effect size having moved towards a certain direction. In detecting the outliers in this study, r-student test was calculated to obtain the specific Z-values where the study whose absolute Z-value exceeded 2, was considered an outlier. A Leave out one analysis was also carried out, whereby the result of the Meta-analysis was re-calculated k-1 time every time leaving out a single study to test the influence of each study on the overall effect. This is the squared Pearson residuals which in other words is the individual contribution to the overall heterogeneity basing on the results from

Cochran's Q-statistic[Baujat et.al.,2002].The study which appears to show an effect size that deviates from the mean on the forest plot is considered an outlier,however this does not automatically mean that it has a greater influence on the pooled effect.

The results from the diagnostic tests represented by graphs showed the influence caused by the individual studies.The DIFFITS indicates the extent to which the pooled effect changes in terms of standard deviations after excluding a specific study[Debray et.al,2018].The cook.d is more the same as the Mahalanobis distance,which is defined from the outlier detection in multivariate statistics as the distance between the value of estimated value when the study is included and when it is excluded [Debray et.al,2018].The Co variance ratio,is the determinant of the variance -covariance matrix of the parameter estimates when the study is removed divided by when the determinant of the variance co-variance matrix of the estimates considering a full dataset [Debray et.al,2018].The value of Cov.r which is less than 1 indicates that removing the estimating will lead to a more precise estimation.

4 Results

4.1 Descriptive statistics

The studies involved seventeen studies carried out in different areas in Kenya and also involving different sets of age groups. All the studies that data was extracted from had a cross-sectional design except one study that was prospective. Approximately 47% of the studies included had been carried out in Nairobi. Most of the studies were carried out in an hospital setting, inpatient, outpatient and psychiatric clinics and a few in schools. 84% of all the studies were carried out on both genders. All the conclusions were drawn assuming a 95% level of confidence. Anxiety disorders showed to co-exist highly with Major Depressive

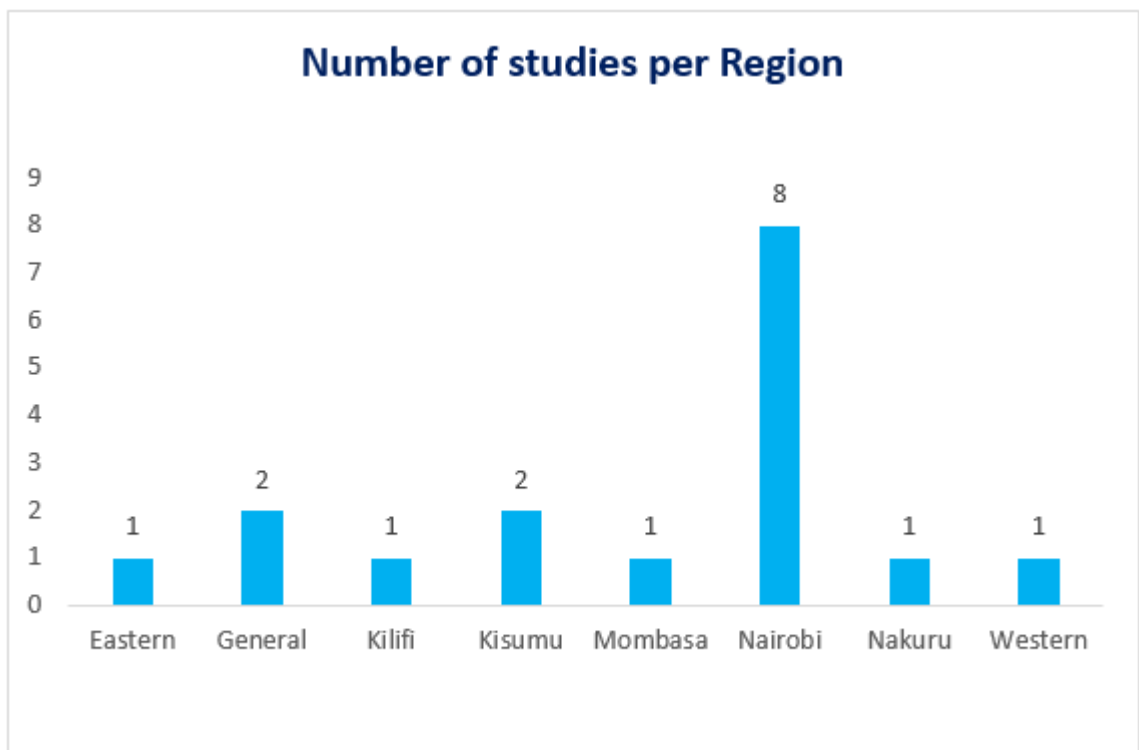


Figure 3. Regions covered in the studies

disorder, Somatoform, suicidality and substance use disorders.

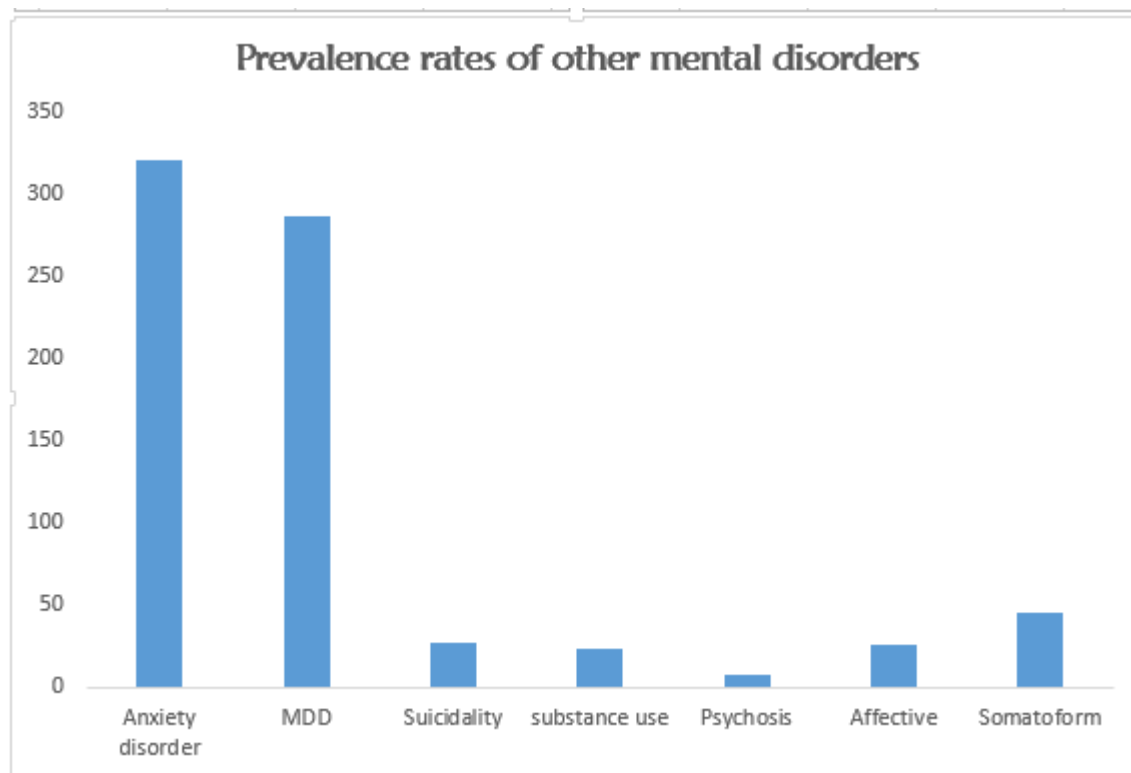


Figure 4. Prevalence of other disorders in the studies included

4.2 Pooling of summary effect

The prevalence rates were pooled to obtain the summary effect size and results were recorded for both Logit and Double arcsine transformations.

	Pooled prevalence	CI.LB	CI.UB
Double Arcsine transformation	0.28594	0.15353	0.44017
Logit transformation	0.27479	0.16197	0.42622

The summary effect sizes had very slight differences. The overall prevalence rate for anxiety disorders is 28.6% with 95% confidence intervals (15.3% ,44.0%) basing on Double arcsine transformation and 27.5% prevalence rate with 95% confidence intervals basing on logit transformation.

4.3 Random effects model

	Estimate	SE	z	p-value	ci.lb	ci.ub
Logit transformation	-0.9704	0.3435	-2.8255	.0047	-1.6436	-0.2973
Double Arcsine transformation	0.5655	0.0818	6.9141	.0001	0.4052	0.7257

The value estimate for the random effects model was -0.9704 for logit transformation and 0.5655 for Double arcsine transformation .The 95% predictor intervals were (-1.6436,-0.2973)and (0.4052,0.7257) and the respective p-values were 0.0047 and 0.0001.

4.3.1 Forest plot

The forest plot below shows the individual standard error,confidence intervals,weight,Heterogeneity measures including predictor interval represents our data in a more digestible format.

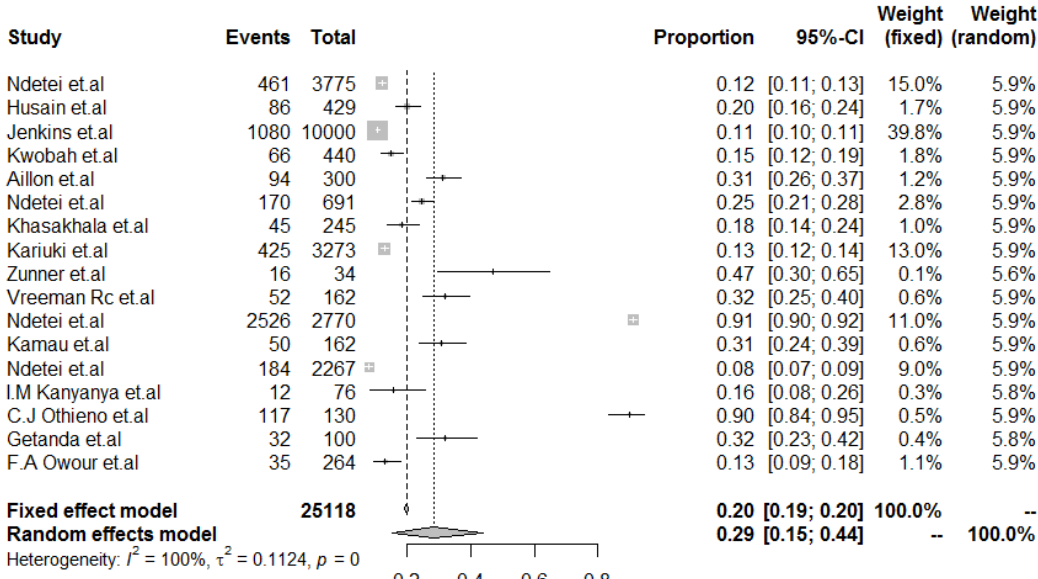


Figure 5. Forest plot without subgroups

The function plotted with a diamond shows where the summary proportion lies,together with the 95% predictor intervals (0.15 ,0.44).The interval does not include zero,hence implies the significance of the model. τ^2 ,0.1124 which is the estimated amount of the total heterogeneity.The weights assigned to the specific studies under fixed effects model varied while the weights under random effects model were approximately uniform.

4.3.2 Heterogeneity Measures

The the three tests for heterogeneity showed a substantial heterogeneity. The Q-statistic, with 16 degrees of freedom was 8825.93 and the p-value of less than 0.0001. The same value was obtained for all the estimates when Dersimonian Laird method and when The Hartung-Knap-Sidik-Jonkman method was considered.

	Estimate	LCL	UCL
τ^2	0.11	0.04	0.19
τ	0.34	0.21	0.44
$I^2\%$	99.82	99.35	99.89
H^2	551.62	220.44	933.52

The table shows heterogeneity measures together with their confidence intervals. The value of I^2 implies that approximately 99% of the total variance is between studies. Whereby the total variance is τ^2 is approximately 0.11 with a lower and upper limits of 0.04 and 0.19 respectively. All the predictors suggest a substantial heterogeneity. The predictor interval (0.4052, 0.7257), which is reliable in drawing conclusion on heterogeneity do not include zero. However, we have find the source of this variance by finding the outlier studies that are responsible for the substantial variability.

4.4 Outlier and Influence Analysis

The test to identify outliers was carried out to ensure the pooled proportion do not depend highly on a single study more than others. Several tests were carried to ensure there is no particular study that pushed our summary effect towards a certain direction and also to identify whether there is a study that caused the substantial heterogeneity.

4.4.1 R-student test

The z-values for every study was less than absolute 2 except for studies 11 (6.8687) and 15 (2.0979) the tow studies were hence considered as the outliers.

float According to this test, study 11 and study 15 are the outliers hence might or might not be responsible for the variation

	Residual	Standard error	Z-value
11	0.7590	0.1105	6.8687
15	0.7208	0.3436	2.0979
13	-0.2938	0.3647	-0.8054
5	-0.3664	0.6895	-0.5313
3	-0.2453	0.4037	-0.6078
17	-0.2027	0.3498	-0.5770
1	-0.2216	0.3841	-0.5770
9	0.2027	0.3561	0.5691
8	-0.2092	0.3798	-0.5508
4	-0.1772	0.3511	-0.5045
14	-0.1601	0.3512	-0.4559
7	-0.1285	0.3498	-0.3673
2	-0.1067	0.3512	-0.3038
6	-0.0490	0.3536	-0.1385
10	0.0404	0.3494	0.1156
16	0.0400	0.3502	0.1143
5	0.0311	0.3497	0.0890
12	0.0264	0.3495	0.0755

4.4.2 Leave-out one Analysis

The result of the Meta-analysis was recalculated K-1 times, each time leaving out one study and the results displayed on the forest plot below. This made it easy to know which study had a greater influence to the overall effect and also if the influence had a significant or negligible impact on the pooled effect.

Each box in the figure above indicates a summary proportion estimated when a specific study is left out. The line at the centre, is the reference line, representing the summary proportion. The further the box deviates study which deviates the greater the impact of the corresponding missing study is on the overall proportion.

4.4.3 Diagnostic tests

The r-student, represented in the graph showed that studies 11 and 15 had the z-values greater than $|2|$. The cooks distance showed that the difference between the result when

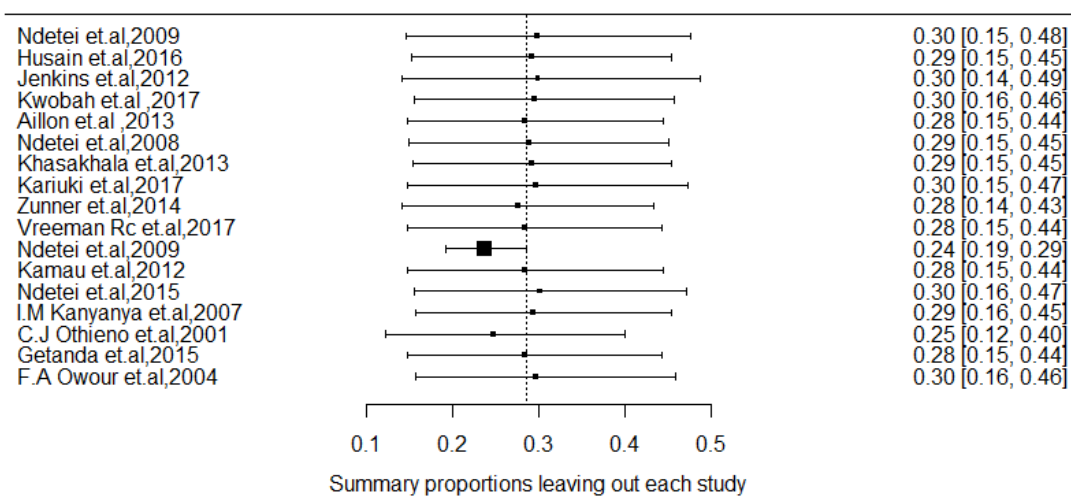


Figure 6. Leave out one analysis

studies 11 and 15 were included and when they were excluded was very different as compared to the rest of the studies. The DIFFTS graph shows that studies 11 and 15 had a greater influence in terms of standard deviations when they were excluded from the overall calculation. The variance co variance graph also showed study 11 showing the greatest influence.

Since both outlier and influential analysis point towards the same direction, the estimates with the reduced data set are as below;

4.4.4 Sensitivity analysis

Basing on the outlier and influential analysis above study 11 and 15 were exempted and analysis carried out.

	Overall Prevalence rate	CI.LB	CI.UB
Reduced data set	25.12 %	19.32%	31.40%
Full data set	28.6%	15.3%	44.0%

Table 1. Sensitivity analysis; Pooled effect

There is a great change in overall prevalence rate with confidence interval implying the significance of the model at 95% confidence interval. The heterogeneity measures also

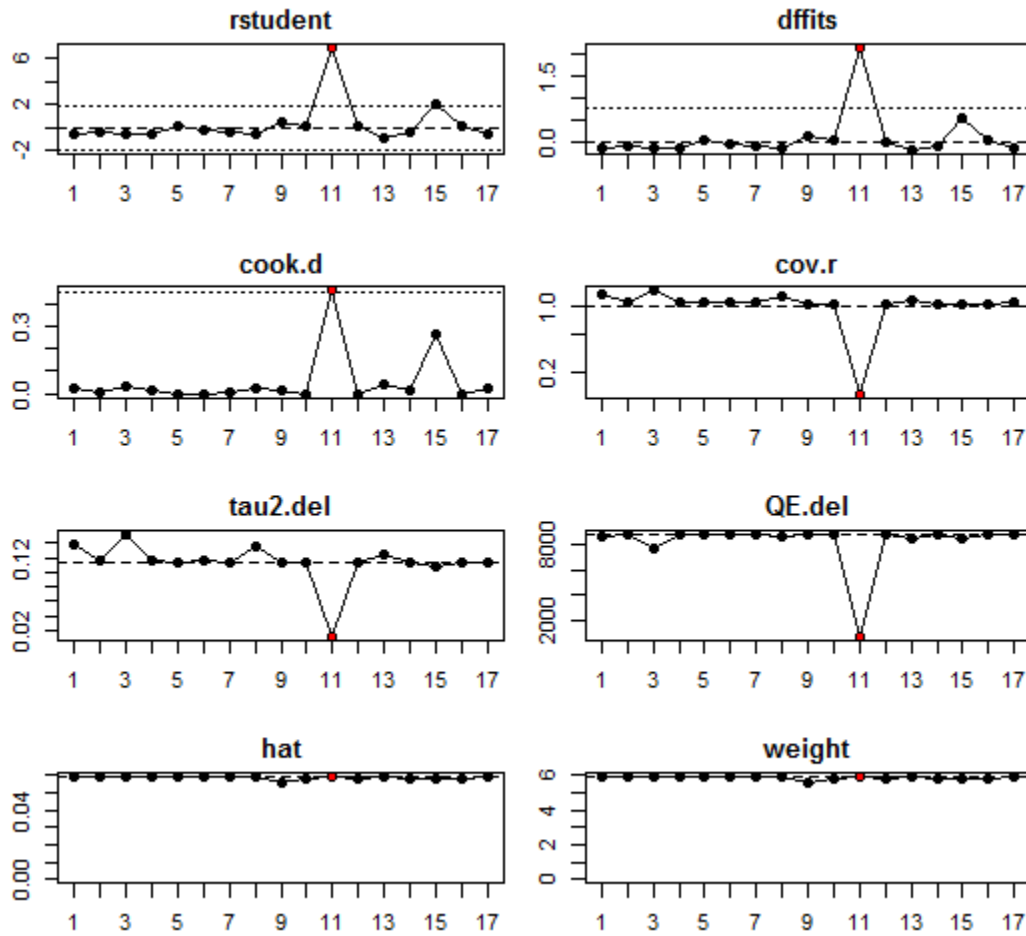


Figure 7. Influence Analysis

differed significantly.

	τ^2	I^2	H^2	Q
Full data set	11%	99.82%	551.62	8825.92
Reduced data set	2%	97.99%	49.82	697.43

Table 2. Sensitivity analysis; Heterogeneity Measures

There is a difference on both the pooled prevalence rate and the heterogeneity measures. The confidence intervals and the p-value for Q-statistic remained at 0.0001.

4.5 Moderator analysis

The results below were obtained from meta-regression of all the moderator variables included in the studies assuming a common among study variance and using the Restricted Maximum likelihood (REML) method which uses likelihood function calculated from trans-

formed set of data ensuring that nuisance parameters have no effect. Individual variables with subgroups were tested for influence on heterogeneity and also on the overall prevalence rate.

Region

The Region in which the studies were carried out showed significant association with the overall proportion. $QM(7)=7.73360$ with $p\text{-value}0.0001$. The specific regression coefficients for the different regions were insignificant except for the studies carried out on General regions. $R^2 = 49.95\%$ of the true heterogeneity was explained for by the moderator variable region and 59.04% of the amount of heterogeneity was not explained by the variable.

	Estimate	se	zval	pval	ci.lb	ci.ub
intercept	-2.4266	0.9971	-2.4338	0.0149	-4.3808	-0.4724 *
Region General	2.8493	1.2300	2.3165	0.0205	0.4385	5.2602 *
Region Kilifi	0.5243	1.4089	0.3722	0.7098	-2.2371	3.2858
Region Kisumu	1.2564	1.2314	1.0203	0.3076	-1.1571	3.6699
Region Mombasa	1.0432	1.4131	0.7383	0.4604	-1.7264	3.8129
Region Nairobi	1.5769	1.0588	1.4893	0.1364	-0.4984	3.6522
Region Nakuru	1.6729	1.4242	1.1746	0.2401	-1.1185	4.4642
Region Western	0.6920	1.4143	0.4893	0.6246	-2.0799	3.4639

Year of Publication

The year in which the studies were published showed no association with the overall effect, $QM(1)=2.4060$, $p\text{-val}=0.1209$ which was also supported by the insignificant regression co-efficient, -0.1164 with confidence intervals $(-0.2634, 0.0307)$. The amount of heterogeneity of the true effect explained by the Year of publication was 0.47% .

Model Results:

	estimate	se	zval	pval	ci.lb	ci.ub
Intercept	233.1193	150.9155	1.5447	0.1224	-62.6697	528.9084
Year	-0.1164	0.0750	-1.5511	0.1209	-0.2634	0.0307

Table 3. Year of publication

Gender

There was no evidence that gender was associated with the overall effect size, $QM(2)=0.2717$, p -value=0.8730. The studies that had both Genders were the reference. The regression coefficients for Female gender (0.1842) and Male gender (-0.2737) had the 95% confidence intervals (-1.9714, 2.3399) and (-0.36992, 2.2518) respectively, confirming no association with the pooled prevalence. $R^2 = 0.00\%$ meaning Gender was not accountable for the overall heterogeneity.

Age group

The age sets involved in the study had no association with the overall effect size, $QM(13)=6.1380$, p -value=0.94. This was also clear in the regression model, none of the age ranges had a significant coefficient of regression. Age sets also explained 0% of the true heterogeneity.

Set up environment for the study

The set up (schools, hospitals, prison, households) where the studies were carried out had no significant correlation with the overall proportion. $QM(11)=10.7380$, with p -value=0.4655. This moderator however explained 20.15% of the overall heterogeneity of the study.

Group of people involved in the study The studies meta-analyzed had been done on different subjects others being Children, adults, Youths, e.t.c. The meta-regression however showed that the group involved was not a significant moderator. $QM(6)=4.2242$ and p -value=0.6464.

Sample size

The sample sizes of the individual studies were not significant moderators, $QM(1)=0.6879$ with p -value=0.4064 this was also evident on its coefficient of regression which turned out insignificant, -0.0001 with 95% confidence interval (-0.0004, 0.0002).

4.6 Publication Bias

Publication bias, which is also known as file-drawer states that a study with low effect size [Rothstein et.al, 2016]. Hence studies with low effect sizes tend to be neglected and never get published. In order to investigate this kind of bias in our studies, several were carried out.

4.6.1 The Funnel plot

This is the best way to visualize whether publication bias exist or not. When there is no publication bias, all studies lie symmetrically around our pooled effect size (where the striped line is). When the publication bias is present the funnel plot would look asymmetrical since only the small studies with large effect sizes are published while small studies with in

significant large effects would be missing [Debray et.al,2018]

The y-axis shows the standard error of each study, where large studies tend to have a

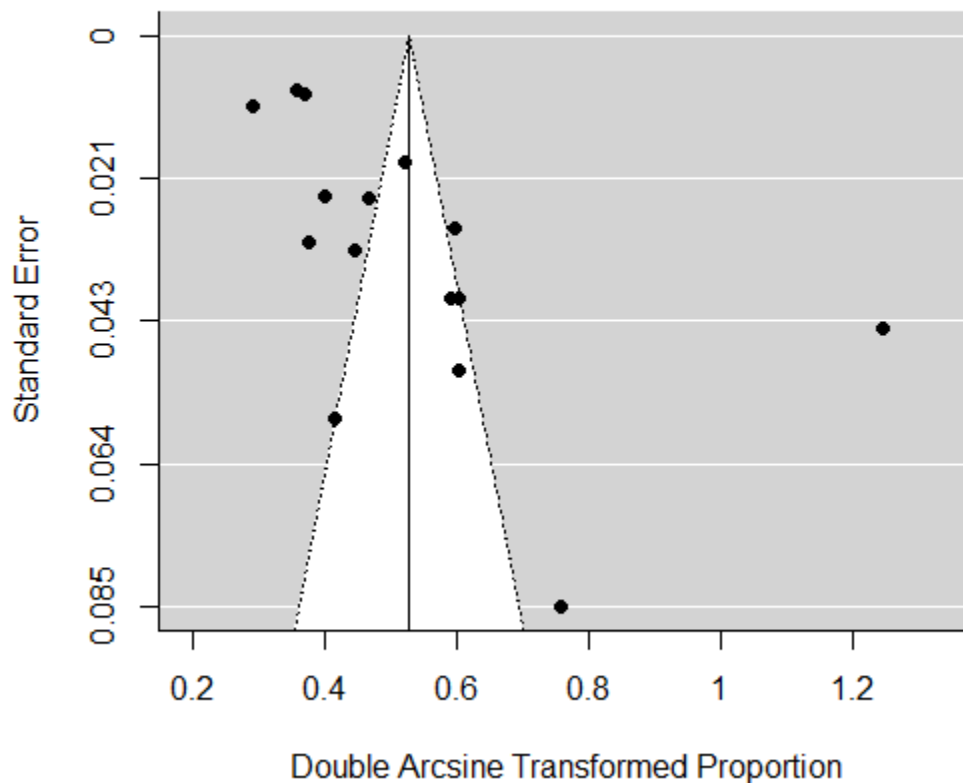


Figure 8. Funnel plot

small standard error and a small effect to the overall proportion The funnel plot is asymmetrical, and most interestingly the two outlier studies are the ones causing the asymmetry of the funnel plot. If there was no bias, then all the studies would lie symmetrically around the pooled effect. Only small studies with large effects might have been published ignoring small studies with insignificant or very small effect sizes. This observation however is not conclusive, hence we carried out some tests to quantify the plot asymmetry.

Eggers test

The Egger's test, using the weighted dispersion with multiplicative dispersion model with the standard error as the predictor value, returned an estimate of $t=3.4418$ with the p -value of 0.0044. Since the p -value obtained was less than the level of significance p -value 0.05, then we conclude that Egger's test was significant implying substantial asymmetry of the funnel plot which is mainly caused by publication bias.

Rank Correlation test

The Kendall's tau value =0.2647,p-value of 0.1513 which is insignificant meaning there is no evidence that we had publication bias basing on the .However,this is not conclusive due to the difference with the former test,and also because Rank correlation test has low power in detecting bias in small studies.

Duval and Tweedies trim and fill procedure

Since publication bias is evident from the above funnel plot and also Eggers test.We then went ahead to find the actual event size supposing the missing studies had been published.The trim and fill procedure imputed the missing studies in the funnel plot until symmetry is achieved.The results were pooled including the imputed and trimmed studies and the actual prevalence rate was obtained for reporting.

The following results were obtained after the trim and fill process;

The value of τ^2 was 1.9743 , I^2 =99.62%,implying the publication bias did not have an

overall proportion	CI.LB	CI.UB
0.2512	0.1932	0.3140

Table 4. Overall proportion after trim and fill

impact on degree of heterogeneity measures.Substantial heterogeneity was evident even in the Q-statistic where its p-value .0001 remained the same even after the bias was rectified.

4.7 Discussion

The data extraction process showed that studies had been carried out across the regions in Kenya except that most studies had not been carried out in rural settings.Majority of the studies had been carried out in Nairobi and involving patients of the same gender. Alongside Anxiety disorders were other mental disorders which co-existed patients suffered from.A majority of the subjects involved in the various studies also suffered from Major depressive disorder,Somatoform,substance abuse and suicidality .It was also noted that one would suffer from more than one anxiety disorder at the same time.

The overall prevalence rate at 95% confidence interval was 28.59%(15.35%) considering a logit transformation and 27.48%(16.2%,42.62%),implying a slight difference between the two methods of transformations.The estimates obtained from the random effects model showed the significance of the model,with p-value 0.0001 and the predictor intervals (0.4052,0.7257)did not include zero.The weights assigned to each study under the random effects model appeared to be even as compare to the weights under fixed effects model. Substantial heterogeneity was observed from all the three measures of heterogeneity.The p-value for the Q statistic was < 0.0001 while the value of I^2 was 99 %.However we could not rely entirely on I^2 since it is highly dependent on the precision of the studies and hence is the amount of variability not explained by the sampling error while on the other

hand, the Q statistic is highly dependent on the size of the Meta-analysis, hence we could not rely fully on these tests to assess heterogeneity due to their high dependence on the statistical power of the study. However since a random effects model was assumed and the predictor intervals implied significance, conclusions were drawn from the study. Study 11 and 15 consistently showed to be the outliers in the study and the diagnostic tests showed that they had a significance impact on the overall effect and also some degree of heterogeneity across studies. The sensitivity analysis carried out after the exemption of the two outlier studies showed a pooled prevalence rate of 25.12% and a 95% confidence interval of 19.32% and 31.40%. The value of variance not explained by the sampling error reduced to 97.9%, implying the two studies explained some degree of between study variance.

The estimate for the model shows confidence intervals that do not include zero on both instances hence shows significance of the model. The p-values are less than the 0.05, implying the model is significant. The confidence intervals are also the predictor variables. The results obtained from the meta-regression showed that the region in which the individual studies had been carried out had a significant association with the summary prevalence rate. It also explained the observed heterogeneity. The gender and the age group included in the specific studies had no evidence of association with the overall effect size and did not explain the observed heterogeneity. This implies that there is no difference in the rates of Anxiety disorders across genders and the different ages in Kenya as suggested by other studies carried out earlier, hence anybody is at a risk of developing Anxiety disorders no matter the age or gender.

The environment or the set-up in which the study was carried out explained the heterogeneity observed but there was no evidence of association with the summary prevalence. The subjects included in the individual studies did not affect the summary effect and also was not accountable of the variance between studies. The sample sizes of each study had no influence on the summary effect, this might be because the studies had been assigned weights fairly hence the studies with larger sample sizes could not dominate the study. The funnel plot was asymmetrical which implied existence of publication bias. There were no studies at the left and lower part of the funnel plot while majority of the studies fell at the left and upper part of the funnel plot. This suggests that small studies (with large standard error) with small effect sizes might have been neglected hence did not have a chance to get published while large studies (small standard error) with small effect sizes had been published anyway might be because of the resources and time spent in carrying out the studies. Small studies with large effect sizes were also missing.

The Egger's test quantified the funnel plot with the value $t=3.4418$ and the p-value = 0.0044 implying a substantial symmetry. The rank correlation test could not be due to its low power in detecting asymmetry in small studies. The trim and fill process was carried out to evaluate the pooled variance in the event that all the documents had been published hence available for the Meta-analysis was. The summary prevalence rate was 25.12% which was exactly what we got after exempting the outlier studies.

4.8 Conclusion

The meta-analysis to pool the different studies that have been done by different people, in different places, with different sample sizes was successful. Measuring the frequency of occurrence of diseases across the globe entails different challenges hence carrying out studies considering a small area could lead to a more precise estimates that could be useful in informing decisions and policies. It was observed that data and information available for mental disorders are still minimal hence the small number of studies involved in the meta-analysis. The data extraction process revealed that most of the studies had been conducted in Nairobi and very few in other parts of Kenya while other parts had never had the study of the same nature being carried out. Many factors can affect the prevalence rates of anxiety disorders as shown from the studies and as proved by the studies included, Anxiety disorders could exist with other serious mental disorders and could also recur in an individual's lifetime.

4.9 Future Research

This study majorly looked at the pooled effect and the reliability of the published documents. We would recommend that the future studies be conducted to focus on other measures of disease occurrence, checking on the risk factors of Anxiety disorders. Since the studies done have only been examining the frequency of anxiety disorders at one point and time, we would recommend a prospective study that will help tell whether the amount of time a patient would need to fully recover from anxiety disorders given a certain treatment or therapy and at what point of the illness is one prone to developing other mental disorders.

z The level of awareness of the existence of Anxiety disorders need to be examined as many people go unnoticed or ignored until the disease gets to unmanageable levels by the patients.

Finally, since Anxiety disorders are risk factors for other diseases, future research on its association with morbidity especially accompanying a lifetime disease would really help to shape the health policy.

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