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Fitting a Model for the Determinants of Breast Cancer in Women Using Meta-Regression

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Abstract: *Meta-regression analysis is a robust statistical framework which is use to examine the relationship between breast cancer determinants and the disease outcomes by combining evidence from multiple studies. This paper aims to fit a model of the determinants of breast cancer using random effect model. The effect size index was odd ratio and data was sourced via Pubmed, Science Direct, Medline, Rechargegate and Google scholar. The random-effects model was employed for the analysis. odd ratio was used as a measure of the association of breast cancer determinants in women. It was formed that the reported* I^2 *statistic is 0.23(23%), which suggest no heterogeneity using the categorization of Higgins et al (2003). In other words, 28% of the variability in the residuals is still attributed to the between-study variation, whereas only 72% is attributed to the within-study variation. The adjuste* R^2 *statistic is 99.06(99%) which assess the proportion of between-study variance explained by the covariates, here ninety-nine per cent (99%) of the between-study variance is explained by the covariates. The model test which is the* X^2*statistic is 9.59 with p-value of 0.0479 which test that all the coefficients other than the intercepts are equal to zero based on the chi-square* X^2 *distribution with p-1 degree of freedom. This paper concluded that on the basis of the data presented and analyzed, it could be noted that the collated results of the secondary studies show that menarche, menopause and family history of breast cancer were strong risk factor for breast cancer while ever breast was not. This paper recommended that menarche, menopause and family history of breast cancer are strong risk factor for breast cancer and it should be included in sensitization and also client counselling.*

Keywords: meta-regression; funnel plot; breast cancer; Chi-square; Tau-square.

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INTRODUCTION

Meta-regression analysis with is robust statistical framework is use to examine the relationship between breast cancer determinants and the disease outcomes by combining evidence from multiple studies. Meta regression can be defined as a statistical tool that uses regression analysis to explore and explain the relationship or variability among study results, and allow researchers to look into how different studies covariates impact on the effect size from other studies. Studies are included with their corresponding data sets which defined meta-regression analysis, notwithstanding if the response variable is a study-level (or corresponding aggregate) data or individual participant data. If a data set includes summary statistics such as sample mean, effect size or odds ratio it is regarded as aggregate (Wikipedia, 2023). Random effects meta-analysis integrates results from multiple studies while accounting for variability both within and between studies. In this way, true heterogeneity, that is, a level of variability between studies that is higher than what would be predicted by chance is represented by the deviations of individual studies from the centre of the distribution.

Breast cancer remains a major public health challenge with its compounded determinants influencing its incidence and advancement in women. Studies have suggested that specific determinants might be a risk factor or associated with an increased risk of breast cancer in women. Though research findings across studies are often inconsistent due to variations in sample size, methodology and study design. This complicates the understanding of the variability in the relationship between the determinants and breast cancer risk. To address this, advance statistical method is employ to combine previous existing research findings and assess their relationship (risk) if the determinants are risk factor of breast cancer. According to Dehesh et al. (2023), many studies have examined the influence of factors, particularly obesity, on breast cancer in light of the rise in breast cancer incidence over the previous few decades. Evaluating potential impacts of obesity on women's breast cancer risk before and after menopause, as well as across continents, is the goal of this systematic review and meta-analysis. The PubMed, Scopus, EMBASE, and Web of Science databases contained all pertinent literature published between January 1, 1990, and January 13, 2023, exploring any potential link between obesity and breast cancer. This included cohort, case-control, and cross-sectional studies. Obesity was classified as having a body mass index (BMI) > 30. Jiryoun et al. (2020) conducted a summary of the utility estimates for breast cancer and evaluated the relative contributions of the study characteristics to the utility prediction of breast cancer.

MATERIALS AND METHOD

Sample and Sampling Techniques

This study consists of a cross-section of breast cancer patients of all age in women. The study was conducted using meta-regression to determine the relationship, variability and to know if this determinants (age at menarche <12, family history of cancer, menopause and ever breastfed) are risk factor for breast cancer in women. The sample of the study consists of 20 effect size from the available registers and records from January 2000 to December 2024 published research findings on determinants of breast cancer in women.

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Methods of Data Collection

For the purpose of this research, secondary data was used, since documented data on women with breast cancer was already published for further research and also data can be access in hard copies in the form of registers that were well documented.

Technique for Data Analysis and Model Specification

Meta-regression is an extension to standard meta-analysis that investigates the extent to which statistical heterogeneity between results of multiple studies can be related to one or more characteristics of the studies (Thompson and Higgins 2002). Like meta-analysis, meta-regression is usually conducted on study-level summary data, because individual observations from all studies (often referred to as individual patient data in medical applications) are frequently not available.

Studies were included in the analysis if they met the following criteria:

i. Already infected with breast cancer disease.
ii. Currently on treatment.
iii. Exposed to risk factors.

For simplicity odd risk (OR) was used as a measure of the association of breast cancer determinants in women.

Model characteristics

Meta regression constitutes an effort to explain statistical heterogeneity in terms of study-level variables, thus summarizing the information not as a single value but as functions. This summary focuses either on the fixed or random effects meta-regression.

Fixed-effects meta-regression

$If\ \widehat{\theta_i} \sim N(\theta_{i,}\ \widehat{\sigma_i}^2)$ (3.1)

Where;

θ_i = the true effect size for study

$\widehat{\theta_i}$ = estimated effect size.

$\widehat{\sigma_i}^2$ = the variance of $\widehat{\theta_i}$.

In fixed-effect meta-regression (Greenland 1987), the study-specific mean, θ_i , is expressed as

$\theta_i = \beta_0 + \beta_1 x_{1_i} + \beta_2 x_{2_i} + \ldots + \beta_{p-1} x_{p-1,i} = x_i\beta \ldots$ (3.2)

Where;

$x_i = (1, x_{1_i}, \ldots, x_{p-1,i})$ Is a 1 x p vector of categorical and continuous moderators (covariates).

β = p × 1 vector of regression coefficients to be estimated.

Or equivalently;

$Effect\ size_i = \beta_0 + \beta_1 Covariate_{i1} + \beta_2 Covariate_{i2} + \ldots + \beta_p Covariate_{ip} + \varepsilon_i$

Where;

$Effect\ size_i$ = The effect size for study

β_0 = The intercept of the meta-regression model.

$\beta_1, \beta_2, \ldots, \beta_p$ = Are the regression coefficients for the predictor variables $(Covariate_{i1}, Covariate_{i2}, \ldots, Covariate_{ip})$.

ε_i = The residual error for study assumed to be normally distributed with zero mean and variance τ^2, where τ^2 is the residual variance which is typically not included in fixed effect meta-regression.

The Vector of Estimated Coefficients

The vector of the estimated regression coefficients, $\hat{\beta}$, includes all the estimated coefficients from the meta-regression model:

$$\widehat{\boldsymbol{\beta}} = \begin{bmatrix} \hat{\beta}_0 \\ \hat{\beta}_1 \\ \hat{\beta}_2 \\ \cdot \\ \cdot \\ \cdot \\ \widehat{\beta_p} \end{bmatrix}$$

Where:

$\widehat{\beta_0}$ = Estimated intercept.

$\widehat{\beta_1}$, $\widehat{\beta_2}, \ldots, \widehat{\beta_p}$ = Estimated coefficients for the covariates variables.

In fixed-effect meta-regression, the estimated coefficients are computed for each study, is weighted by the inverse of its variance. The fixed-effects model assumes a common effect size and calculates the regression coefficients to minimize the weighted sum of squared residuals.

The Matrix Formulation

Let ϕ be the vector of observed effect size, X be the matrix of covariates variables (with a column of ones for the intercept) and W be the diagonal matrix of weights (inverse variances) then the matrix form of the fixed-effects meta-regression can be express as:

$$\phi = X\beta + \varepsilon \qquad (3.3)$$

Where:

$\boldsymbol{\phi}$ = n x 1 vector of effect sizes.

X = n x (p +1) matrix of predictors, including the intercept.

$\boldsymbol{\beta}$ = (p + 1) x 1 vector of coefficients

$\boldsymbol{\varepsilon}$ = n x 1 vector of residuals.

The weighted least squares (WLS) estimate of $\boldsymbol{\beta}$ is:

$$\widehat{\beta} = (X'\mathrm{WX})^{-1}X'W\hat{\phi} \qquad (3.4)$$

Where:

W = diag.$(w_1, w_2, \ldots, w_p)$.

Random-effects meta-regression

According to Berkey et al.(1995) random-effects meta-regression model may be defined as:

$$\widehat{\phi_\iota} = x_i\beta + u_i + \varepsilon_i \qquad (3.5)$$

Where:

ϕ_i = Estimated effect sizes.

x_i = n x (p + 1) matrix of the predictors.

β = (p + 1) x 1 vector of coefficients.

$u_i \sim N(0, \tau^2)$.

$\varepsilon_i \sim N\left(0, \widehat{\sigma_\iota^2}\right)$.

Random-effects meta-regression first estimate the between-study variance, τ^2 and the regression coefficients are then estimated via weighted least squares.

$\widehat{\beta^*} = (\mathrm{X}'W^*\mathrm{X})^{-1}\,\mathrm{X}'\mathrm{W}^*\hat{\phi}$ (3.6)

Where:

$\mathrm{W}^* = diag(w_1{}^*, w_2{}^*, \ldots, w_k{}^*)$ and $w_i{}^* = (1/_{\sigma_i{}^2} + \widehat{\tau^2})$.

Or equivalently

$Effect\ size_i = \beta_0 + \beta_1 Covariate_{i1} + \beta_2 Covariate_{i2} + \ldots + \beta_p Covariate_{ip} + u_i + \varepsilon_i$

Where;

$Effect\ size_i$ = The effect size for study

β_0 = The intercept of the meta-regression model.

$\beta_1, \beta_2, \ldots, \beta_p$ = Are the regression coefficients for the predictor variables $(Covariate_{i1}, Covariate_{i2}, \ldots, Covariate_{ip})$.

u_i = The random effect specific to study, which accounts for the between-study variability in the effect size.

ε_i = The residual error for study assumed to be normally distributed with zero mean and variance σ^2.

The Variance Components

The total variance of the effect size is decomposed into two in random-effects model.

i. Between-study variance (τ^2), which is the variability in the true effect sizes across studies.
ii. Within-study variance (σ^2), which is the variability within each study.

The variance of the effect size for study is given as:

$\mathrm{Var}(\phi_i) = \sigma^2 + \tau^2$ (3.7)

The weighted regression is estimated from the random-effects meta-regression model since the model accounts for both within-study and between-study variances.

3.4.2.2 The Vector of Estimated Coefficients

In random-effects meta-regression, the vector of estimated regression coefficients is:

$$\widehat{\boldsymbol{\beta}^*} = \begin{bmatrix} \hat{\beta}_0 \\ \hat{\beta}_1 \\ \hat{\beta}_2 \\ \cdot \\ \cdot \\ \cdot \\ \widehat{\beta_p} \end{bmatrix}$$

Where:

$\widehat{\beta_0}$ = Estimated intercept.

$\widehat{\beta_1}, \widehat{\beta_2}, \ldots, \widehat{\beta_p}$ = Estimated coefficients for the covariates variables.

The weight for each study in random-effects meta-regression is computed as:

$w_i = \frac{1}{\sigma^2 + \tau^2}$ (3.8)

Where:

σ^2 = The within-study variance.

τ^2 = The between- study variance.

Both the σ^2 and τ^2 need to be estimated either from Restricted Maximum Likelihood (REML), Dersimonian-Laird Method, Method of Moment or Empirical Bayes Methods.

Permutation test

Higgins and Thompson suggested using the permutation test method to determine the p-values in meta-regression. The permutation test offers a nonparametric method for simulating data under the null hypothesis (H_0). If there are few studies that used Monte Carlo simulation, which is based on random permutations rather than a list of all possible permutations, it would be able to get the exact permutation p-values. A t statistic is computed for each time the variables are randomly reallocated to the outcomes. The number of times these t statistics are larger than or equal to the observed t statistic is counted to determine the true p-value for the association between a given covariate and the response. The covariate values for a particular research are retained when numerous variables are included in the meta-regression in order to maintain and account for their correlation structure. Unlike other regressions, the output of a meta-regression comprises of the effect size and its standard error, which need to be retained.

$$p\,(\,t \geq t_0) = \frac{1}{(n+m)!}\Sigma_{j=1}^{(n+m)!}\, I\,(t_j \geq t_0) \qquad (3.9)$$

Where;

t_0 = observed value of the test statistic

t = t- value.

I = indicator function

Given the significance level (α = 0.05), we fail to reject the Null (H_0) hypothesis if the p – value is greater than alpha.

Knapp-Hartung Variance Estimator

To account for between-study variance, the Knapp-Hartung variance estimator modifies the standard errors of the computed coefficients in meta-regression. When there is significant heterogeneity or a small number of studies, this technique yields a more reliable estimate of the variance. To estimate the between-study variance (τ^2), methods like Restricted Maximum Likelihood (REML) or Dersimonian-Laird Method is used and this estimate is used to adjust the weights in the meta-regression model.

Knapp-Hartung Variance Estimate for Coefficient

Let $\widehat{\beta_k}$ be the regression coefficient then the Knapp-Hartung variance estimator $\widehat{V_{KH}}(\widehat{\beta_k})$ is computed as:

$$\widehat{V_{KH}}(\widehat{\beta_k}) = \widehat{V_{FE}}(\widehat{\beta_k}) \text{ x } \left[1 + \frac{1}{n}\left(\frac{\sum_{i=1}^{n} w_i}{\sum_{i=1}^{n} w_i^2} - \frac{1}{n}\right)\right] \qquad (3.10)$$

Where:

$\widehat{V_{FE}}(\widehat{\beta_k})$ = Fixed-effects variance estimator for $\widehat{\beta_k}$.

w_i = weights for each study.

n = the number of studies.

Knapp-Hartung Adjustment for Confidence Interval (CI):

The confidence interval for the coefficient $\widehat{\beta_k}$ can be adjusted using Knapp-Hartung variance estimate:

$$CI_{KH}(\widehat{\beta_k}) = \widehat{\beta_k} \pm z_{\alpha/2}\sqrt{\widehat{V_{KH}}(\widehat{\beta_k})} \quad (3.11)$$

Where:

$z_{\alpha/2}$ = Critical value from the standard normal distribution for the confidence level (1.96 or 95% CI).

Knapp-Hartung t-Test Statistic

The t-test statistic using the Knapp-Hartung variance estimator is:

$$t_{KH} = \frac{\widehat{\beta_k}}{\sqrt{\widehat{V_{KH}}(\widehat{\beta_k})}} \quad (3.12)$$

Where:

$\widehat{\beta_k}$ = The estimated regression coefficient.

$\sqrt{\widehat{V_{KH}}(\widehat{\beta_k})}$ = The standard error from Knapp-Hartung variance.

ANALYSIS AND RESULTS

Fitting a model of the determinants of breast cancer using random effect model.

Table 1.0: showing determinants of breast cancer using random effect model.

```
  Effect-size label: Effect size
        Effect size: lnor
          Std. err.: selnor

Random-effects meta-regression                  Number of obs  =        20
Method: DerSimonian-Laird                       Residual heterogeneity:
                                                          tau2 =  .00041
                                                       I2 (%)  =    0.23
                                                          H2   =    1.00
                                                R-squared (%)  =   99.06
                                                Wald chi2(4)   =    9.59
                                                Prob > chi2    =  0.0479
```

_meta_es	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
menarche	.0948174	.1537927	0.62	0.538	-.2066107	.3962455
everbreastfed	-.3956679	.2081213	-1.90	0.057	-.8035782	.0122424
menapause	.1318427	.0887161	1.49	0.137	-.0420376	.3057231
familyhistoryofbreastcancer	.2404568	.1736986	1.38	0.166	-.0999863	.5808998
_cons	-7.498441	4.926519	-1.52	0.128	-17.15424	2.157358

```
Test of residual homogeneity: Q_res = chi2(15) = 15.03   Prob > Q_res = 0.4489
```

From the above table it shows the output of the random-effect meta-regression analysis of twenty (20) observations of breast cancer determinants in women that were included in the analysis. The header includes the information about the meta-regression analysis model and reports various summaries such

as heterogeneity statistics and the model test. The reported I^2 statistic is 0.23(23%), which suggest no heterogeneity using the categorization of Higgins et al (2003). In other words 28% of the variability in the residuals is still attributed to the between-study variation, whereas only 72% is attributed to the within-study variation.

Assessing publication bias and testing their symmetry using funnel plot

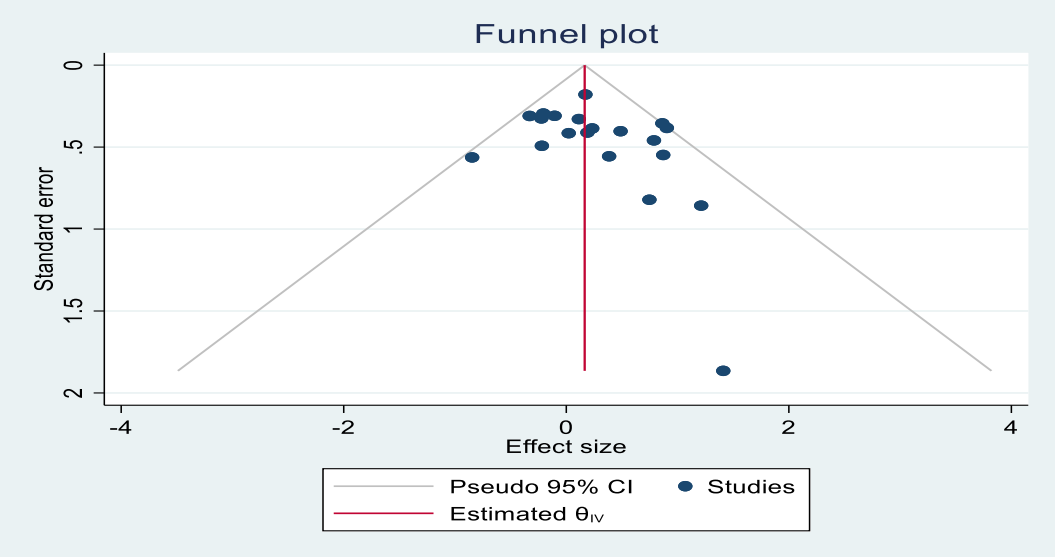

Figure 1.0 Funnel plot of the scattered plot of the natural logarithm of effect-size against their natural logarithm of standard error

DISCUSSION OF FINDINGS

The result of this study support the fact that menarche, menopause and family history of breast cancer are risk factors for breast cancer but ever breastfed was not a risk factor for breast cancer, from table 4.2. The variation was low (23%) which suggested no heterogeneity based on Haggin et al (2003) categorization with the adjusted R^2statistic 99%, which represent the proportion of the variability in the outcome variable that is explained by the predictors(Determinants) included in the model. The X^2statistic is 9.59 with p-value of 0.0479 which typically is used to test the significance of the overall model (Independent variables or determinants) on the outcome variable. Since the p-value is < 0.005, it indicates that the model with the predictors provides a significantly better fit than a model with no predictors (i.e., the determinants in the model help explain the variation in the effect size).
At the bottom of the output table the residual homogeneity is reported, the test statistic is 15.03 with a p-value of 0.4489 which suggest the absence of heterogeneity among the residual. The coefficient of menarche is 0.0948174 with p-value 0.538, which means that for each year earlier the odds of developing breast cancer increases, which suggests that menarche is associated with a high likelihood of breast cancer. The coefficient of ever breastfed is -0.3956677 with p-value 0.057, which means that for each year earlier the odds of developing breast cancer decreases. Which suggests that ever breastfed is associated with a low likelihood of breast cancer. The coefficient of menopause is 0.1318427 with p-value 0.137, which means that for each year earlier the odds of developing breast cancer increases. Which suggests that menopause is associated with a high likelihood of breast cancer.

The coefficient of family history of breast cancer is 0.2404568 with p-value 0.166, which means that for each year earlier the odds of developing breast cancer increases, which suggests that menarche is associated with a high likelihood of breast cancer.

Model:

$$Y = -7.498441 + 0.0948174X_1 - 0.3956679X_2 + 0.1318427X_3 + 0.2404568X_4$$

The funnel plot was use to assess the potential presence of publication bias or small study effects which can influence the results of the analysis. It was combined with statistical models to explore whether certain characteristics (determinants) explain any asymmetry in the funnel plot and from figure 1.0 there is no heterogeneity since the studies are scattered within the confidence interval region which resembles an inverted funnel shape, hence there is no publication bias.

CONCLUSION

On the basis of the data presented and analysed, it could be noted that the collated results of the secondary studies show that menarche. Menopause and family history of breast cancer were strong risk factor for breast cancer while ever breast was not.

Recommendations

Based on the data collated, analysed with the findings, the researcher wishes to recommend the following;

i. Menarche, menopause and family history of breast cancer are strong risk factor for breast cancer and it should be included in sensitization and also client counselling.
ii. Routine check-up should be provided free for all.
iii. Exercise and life style should be part of the foundation stone to help keep our women in good health.

REFERENCES

Adebamowo, C. O., & Ajayi, O. O. (1999). Breast Cancer in Nigeria. *Breast Cancer in Nigeria*.

Afolayan, E. A., Olaoye, O., Adesina, M., & Saidu, R. (2012). Breast Cancer Trends in a Nigerian Population: An Analysis of Cancer Registry Date. *International Journal of Life Science & Pharma Research*.

Aghili, M. M., AFSA, Zare, M. M., Mousavi, N. M., Ghalehtaki, R. M., Sotoudeh, S. M., et al. (2019). Efficacy of gabapentin for the prevention of paclitaxel induced peripheral neuropathy: A randomized placebo controlled clinical trial. *The Breast Journal*.

American Cancer Society. (2020, June 18). Cancer Staging. American Cancer Society. *American Cancer Society*.

Breastcancer.org. (2020, March 28). Tamoxifen: Uses, Side Effects and More. *Tamoxifen: Uses, Side Effects and More.*

Carrara, H. (2017, July 15). Cancer Incidences in Namibia. *Namibia National Cancer Registry*.

Cohen, J. (1977). *Academic Press*.

Cohen, J. (1988). Statistical Power Analysis for the behavioral sciences (2nd ed.). *Academic Press*.

Cordina-Duverger, E., Truong, T., Anger, A., Sanchez, M., Arveux, P., & Guenel, P. (2013, November 1). Risk of breast cancerby type of menopausal hormone therapy: a case-control study among post-menopausal women in France. *Risk of breast cancerby type of menopausal hormone therapy, 8*(11).

Cuzick J et al. (2013). Selective Oestrongen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data. *381*(9880), 1827-1834.

de Blok, C. J., Wiepjes, C. M., Nota, N. M., Engelen, K. V., Adank, M. A., Dreijerink, K. M., et al. (2019, 5). Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands. *BMJ*.

Dehesh, T., Shohreh, F., Mehmaz, S., Elham, A., Mehran, I., Paria, D., et al. (2023). The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis.

Downie, N., & Heath, R. (1974). Basic Statistical Methods (4th ed.). New York: Harper and Row Publishers.

Endemann, G. (2020, October 1). *goop*. Retrieved 5 4, 2024, from goop.com: https://goop.com/wellness/health/breast-cancer/

Adebamowo, C. O., & Ajayi, O. O. (1999). Breast Cancer in Nigeria. *Breast Cancer in Nigeria*.

Afolayan, E. A., Olaoye, O., Adesina, M., & Saidu, R. (2012). Breast Cancer Trends in a Nigerian Population: An Analysis of Cancer Registry Date. *International Journal of Life Science & Pharma Research*.

Aghili, M. M., AFSA, Zare, M. M., Mousavi, N. M., Ghalehtaki, R. M., Sotoudeh, S. M., et al. (2019). Efficacy of gabapentin for the prevention of paclitaxel induced peripheral neuropathy: A randomized placebo controlled clinical trial. *The Breast Journal*.

American Cancer Society. (2020, June 18). Cancer Staging. American Cancer Society. *American Cancer Society*.

Breastcancer.org. (2020, March 28). Tamoxifen: Uses, Side Effects and More. *Tamoxifen: Uses, Side Effects and More.*

Carrara, H. (2017, July 15). Cancer Incidences in Namibia. *Namibia National Cancer Registry*.

Cohen, J. (1977). *Academic Press*.

Cohen, J. (1988). Statistical Power Analysis for the behavioral sciences (2nd ed.). *Academic Press*.
Cordina-Duverger, E., Truong, T., Anger, A., Sanchez, M., Arveux, P., & Guenel, P. (2013, November 1). Risk of breast cancerby type of menopausal hormone therapy: a case-control study among post-menopausal women in France. *Risk of breast cancerby type of menopausal hormone therapy, 8*(11).

Cuzick J et al. (2013). Selective Oestrongen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data. *381*(9880), 1827-1834.

de Blok, C. J., Wiepjes, C. M., Nota, N. M., Engelen, K. V., Adank, M. A., Dreijerink, K. M., et al. (2019, 5). Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands. *BMJ*.

Dehesh, T., Shohreh, F., Mehmaz, S., Elham, A., Mehran, I., Paria, D., et al. (2023). The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis.

Downie, N., & Heath, R. (1974). Basic Statistical Methods (4th ed.). New York: Harper and Row Publishers.

Endemann, G. (2020, October 1). *goop*. Retrieved 5 4, 2024, from goop.com: https://goop.com/wellness/health/breast-cancer/

Fournier, A., Berrino, F., & Clavel-Chapelon, F. (2008, February 27). Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study.breast cancer research and treatment. *National Library of Medicine, 107*(1), 103-111.

Glass, G., & Stanley, J. (1970). Statistical Methods in Education and Psychology. *Englewood Cliffs, N J: Prentice Hall*.

Glass, G., McGaw, B., & Smith, M. (1981). Meta-Analysis in social research. *Sage*.

Haffner, I., Schierle, K., Raimundez, E., Geier, B., Maier, D., Hasenauer, J., et al. (2021, March 28). HER2 Expression, Test Deviations, and Their Impact on Survival in Metastatic Gastric Cancer: Result from the Prospective Multicenter VARIANZ Study. *HER2 Expression, Test Deviations, and Their Impact on Survival in Metastatic Gastric Cancer: Result from the Prospective Multicenter VARIANZ Study*.

Hejmadi, M. (2010). Introduction to Cancer Biology. 2nd Edition.

Javan, B. A., Rafiei, S., Sima, R., Fatemeh, K., Mitra, K., Farzaneh, B., et al. (2023). Global quality of life in breast cancer: systematic review and meta-analysis.

Jiryoun, G., Juhee, H., Donghwan, L., & Seungjin, B. (2020, December 09). A Meta-Regression Analysis of Utility Weights for Breast Cancer: The power of Patients' Experience.

Kelly, K. M., Dean, J., Comulada, S. W., & Lee, S.-J. (2010, March). Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. *Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts, 20*(3), 734-42.

Lipsey, M., & Wilson, D. (2001). Practical Meta-Analysis. *Thousand Oaks, CAUS*.

Lyons, L. (2003). Meta- Analysis: Across Research Domains.

Manson, J. E., Rowan, C. T., Stefanick, M. L., Aragaki, A. K., Rossouw, J. E., Ross, P. L., et al. (2013). Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA*.

Marcucci, R. (1980). A Meta-Analysis of Research of Teaching Mathematical problem solving, Doctoral dissertation. *Dissertation Abstracts International, 41 06A*.

Mayo Clinic. (2018, November 22). Chemotherapy nausea and vomiting: Prevention is best defense. *Chemotherapy nausea and vomiting: Prevention is best defense*.

Mayo Clinic. (2019, November 22). Breast Cancer-Diagnosis and treatment. *Mayo*.

National Cancer Institute. (2015, April 29). Appetite Loss and Cancer Treatment. *National Cancer Institute*.

National Cancer Institute. (2019). Breast Cancer. *Breast Cancer*.

O'Rourke , K. (2007). An historical perspective on meta-analysis: dealing quantitatively with varying study results. *Journal of the Royal Society of Medicine, 100*(12), 579-582.

Rebolj, M., Assi, V., Brentnall, A., Parmar, D., & Duffy, S. W. (2018, June). Addition of ultrasound to mammography in the case of dense breast tissue: systematic review and meta-analysis. *Addition of ultrasound to mammography in the case of dense breast tissue: systematic review and meta-analysis*.

Ronald, C., Charles, S. B., Vicky, R., Leonard, C., & Michael, L. (2021, October 31). Weight changes of younger and older early breast cancer patients - a meta regression. *10*.

Rosenthal, R. (1984). Meta-Analysis Procedures for Social Research. *SAGE Publication Inc*.

Rosenthal, R., & Rosnow, R. (1984). *Methods and Data Analysis. New York, McGaw-Hill*.

stata.com. (2023). *stata.com*. Retrieved June 12, 2024, from www.stata.com.

Thigpen, D., Kappler, A., & Brem, R. (2018, March 16). The Role of Ultrasound in Screening Dense Breasts—A Review of the Literature and Practical Solutions for Implementation. *Diagnostics, 8*(1).

WHO. (2014, February 3). *WHO*. Retrieved from www.who.int: https://www.who.int/news-room/fact-sheets/detail/cancer

WHO. (2022, March 13). *Breast Cancer*. Retrieved May 12, 2024, from World Health Organization: https://www.who.int/news-room/fact-sheets/detail/breast-cancer

WIKIPEDIA. (2023, December 3). *Meta-regression*. Retrieved May 12, 2024, from WIKIPEDIA: https://en.wikipedia.org/wiki/Meta-regression

Young, A., Niekerk, V. C., & Mogotlane, S. (2003). *Juta's Manual of Nursing*. South Africa: juta & co Ltd.