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Research Article

Socio Economic Determinants of Breast Cancer Revalence in Southwestern, Nigeria

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Abstract

Background and Objective: Breast cancer is one of the world's rapidly growing deadly diseases with Africa included. More than 30% of the total prevalence of cancer cases in western Nigeria accounted for breast cancer making it to be the leading public health problem among western of Nigeria. The aim of this study was to investigate the factors associated with histological type of breast cancer and to examine its implications for long-term prognosis. Despite the number of research done on breast cancer, this paper steps further by the use of statistical techniques which may improve the quality of the results. **Materials and Methods:** Multinomial logistic regression analysis was applied to breast cancer data extracted from the cancer registry of Federal Medical Teaching Hospital. Two identical multinomial models were fitted using frequentist and Bayesian with non-informative prior. The software R and Win BUGS are used to implement the analysis. **Results:** The mean age of the participants was 42.2 ± 16.6 years, with 81% presenting with malignant breast lesion. Seventy-one percent were treated with surgery, 52.3% had tertiary education and 41% belong to age group 20-34 years. Patient with at least high school education were 51% more likely to suffer from mastocytosis (posterior odds ratio [OR] = 1.51(95%, credible interval 1.32-8.31). Being Christian (vs. Muslim) was associated with lower odds of lobular carcinoma (OR = 0.68, Cred. I: 0.30-2.28). In contrast, high level of education is independently associated with mastocytosis form of histologic type. In addition, high level of educational status, age, occupation and religion affiliation were significantly associated with histologic type of breast cancer in both techniques. **Conclusion:** In the light of the findings of this study, intervention aimed at curbing the burden of breast cancer should jointly target those patients that are highly educated to take caution to health management. Moreover, the study has provided important information about the breast cancer lesion which may explain the high prevalence among western women. This can contribute to policy development and prevention strategies for breast cancer treatment among western women in Nigeria.

Key words: Breast cancer, Bayesian, multinomial, histologic type, Nigeria

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Breast is a major cause of death among women both in developed and less developed countries and despite improvement in modifiable associated risk factors. This explains why there is still ongoing study to identify the association between other risk factors that may possibly responsible for the growing burden of breast cancer globally. In Nigerian setting, Breast cancer (BC) is the most common type of cancer among women¹⁻⁶, with an overall age standardized rate (ASR) of 52.2 per 100,000 as reported by^{7,1-3,8}. Previous studies affirmed that breast cancer among Nigerian women differs across the states of the federation. For instance, in northern part of Nigeria breast cancer is the second most common diagnosed in women while western part has breast cancer as the most diagnosed cancer among their women⁹.

However, several studies have assessed the risk factors associated with breast cancer and many of them have been identified as established factors. Increasing age has been identified by many studies as risk factors¹⁰. In addition, the use of oral contraceptive^{11,12}, lifestyle factors such as alcohol consumption^{13,14} and high fat diet^{15,16} have been identified by many studies as risk factors for breast cancer. Recently, some studies have shown that histological types of breast cancer is associated with reproductive factors, age at first birth and other hormone related risk factors¹⁷. Nevertheless, no more studies have examined whether particular histologic type of breast cancer have an association with socio-demographic and medical factors. Further knowledge about this issue may add more valuable information for breast cancer prevention and treatment in western Nigeria as a first step to identify which of these factors may be amenable to intervention in the Nigeria setting. This study was therefore, conducted to determine the prognostic implication and risk factors associated with patients diagnosed with different histological grade among women of western Nigeria using Bayesian and classical approaches. Bayesian statistics techniques are currently given high importance in the field of statistics as better option to analyze data. But, the uses of these approaches are still reserved to an elite and the understanding seem complicated due to insufficient literature on its applications. The main difference between Bayesian and classical inference is the introduction of prior information in Bayesian models. This study considers Bayesian models using non-informative prior, where the influence of the prior on the overall model is insignificant.

MATERIALS AND METHODS

The study was approved by Ethic Committee of Federal Medical Teaching Hospital, Ekiti state, Nigeria (ERC/2016/02/25/09B). All the personal information collected was considered confidential. The software R was used for the classical statistical analysis and software WinBUGS 14 for the Bayesian analysis. As a requirement of the Bayesian approach, several diagnostics tests were performed to answer convergence of the Markov chain Monte Carlo algorithm and the true reflection of the posterior distribution.

Statistical model: Data was analyzed by fitting a generalized linear model. The generalized linear model (GLM) generalizes linear regression by relating the outcome variable to predictor variables via a link function. The class of GLM involves many well-known statistical models which include multinomial regression, logistic regression model and so on. The GLM have been extended so as to accommodate both random and mixed effects. The multinomial logistic regression model is classified under GLM. This model is used to model an outcome variable that has more than two categories. For a multinomial logistic regression, a technique of maximum likelihood estimation (MLE) is used to estimate parameters of the model. In addition, the estimates of the parameters and variance covariance matrix can be obtained by any standard statistical computer packages like SAS and R (nnet package).

Bayesian approach: The Markov Chain Monte Carlo (MCMC) is one of the techniques used to generate the estimates of the unknown parameters from appropriate distribution and also corrects the values obtained so as to have a reliable estimate for the desired posterior distribution¹⁸⁻²⁰. The MCMC techniques provide a better alternative to summarize the posterior distribution if the posterior comes from a complex distribution. The most significant aspect in Bayesian is to set up a proper prior to include in the model. In this study, non-informative prior is utilized in the selection of prior for the Bayesian approach. A non-informative prior that will not influence the posterior distribution is chosen by using a normal distribution with a large variance ($\sigma^2 = 1000$) and mean ($\mu = 1$):

$$\beta_i \sim N(1, 10000)$$

The variance (σ^2) is transformed to inverse variance $\tau = 0.0001$ in order to be fitting into the Bayesian model.

Furthermore, to avoid problem of auto-correlation or non-convergence, it is necessary to check for the convergence of the MCMC algorithm. The convergence of the MCMC model parameters were obtained by checking trace plots and auto-correlation plots of the MCMC output²¹.

Characteristics of the study population: A total of 237 women were recruited. The mean age of the participants was 42.2 ± 16.6 years. Out of the 237 participants, 168 (70.9%) had been subjected to surgery treatment, 192 (81.0%) had their breast cancer level as malignant lesion, 124 (52.3%) had attended sec/high school and 99 (41.8%) had infiltrating duct carcinoma. From descriptive statistics, it found that the percentage of patients with highest breast cancer is among those who had at least high school education (Table 1).

Risk factors associated with histologic type: The model was fitted to each predictor variables one at a time. The objective of this paper is to identify the individual risk factors of breast cancer patient that could be associated with the histologic type. On the other hand, this study focused on identifying the individual risk factors which could be associated with the patient having different histologic type. To make statistically valid inferences, the analysis of the data must account for the design of the study. The R software procedure which performs multinomial logistic regression for categorical response in the data was employed in the case of classical statistics. Various predictors including medical factors and socio-demographic factors are included in the model. The predictors introduced in the model are: Age group: 35-49, 50-69, 70+, Occupation: employed/unemployed, Educational status: Primary and no education/at least high school and religion affiliation: Christian and Islamic.

Classical inference results: The results of the socio-demographic risk factors obtained from classical statistics summarized in Table 2 affirmed that age group 35-49 years, 50-69 years, patient with at least high school education, unemployed and religion affiliation were significantly associated with lobular form of histologic type. Findings from this model affirm that some of the other covariates utilized in the model are significant predictors of the risk of histologic type at 95% significant level. The odds of lobular carcinoma were significantly higher among patient aged 50 years and older. For patient aged 35-49 years, findings led to an OR = 3.86 which indicates that they are 3.9 times more likely to suffer lobular carcinoma compared

Table 1: Socio-demographic characteristics of the study population

Demographics	n (%)
Age: n (%)	
Mean $\pm$ SD	42.2 $\pm$ 16.6
20-34	97.0 (40.9)
35-50	72.0 (30.4)
51+	68.0 (28.7)
Education	
At least high school	113.0 (47.7)
Tertiary	124.0 (52.3)
Breast cancer type	
Malignant	192.0 (81)
Benign	45.0 (19)
Treatment type	
Surgery	168.0 (70.9)
Others	69.0 (29.1)
Histological type	
Infiltrating duct carcinoma	99.0 (41.8)
Lobular carcinoma	57.0 (24.1)
Mastocytosis	16.0 (6.8)
Mixed histologic type	65.0 (27.3)

to patient aged 20-34 years. Also, the odd of getting lobular carcinoma in unemployed women was higher by 2.44 times (95%CI: 1.45-5.30) than employed women in either Government or private sectors. Compared to women with primary education, those with at least high school education are at higher risk of mastocytosis form of histologic type by (OR = 10.38, 95%CI: 2.53-17.54) (Table 2).

Bayesian inference results: For the Bayesian approach, WinBUGS software is employed to fit the model. The same covariates as in classical model are included in the Bayesian model but using non-informative prior. The results of non-informative prior Bayesian model show that variables age, education, religion affiliation and occupation are the only significant predictors associated with histologic type of breast cancer. Regarding the effect of age on lobular carcinoma, findings highlight that patient aged 35-49 years are 1.03 times more at risk of lobular carcinoma compared to those in the age group 20-34 years. In addition, the odds of lobular carcinoma were significantly higher among patient 50-69 years compared to patients in age group 20-34 years. Moreover, findings indicated that patient with at least high school education are at higher risk (OR = 1.51, 95% Cred.I: 1.32-8.31) of mastocytosis form of histologic type compared to those with primary school education. Also, women who are diagnosed of breast cancer but they are Christian are 32% (OR = 0.68) less likely to suffer from lobular carcinoma compared to those who practiced Islamic religion. Furthermore, the findings from Bayesian affirm that patient who are unemployed are at higher risk of lobular

Table 2: Multinomial model estimates of risk factors associated with histologic type of breast cancer

Variables	Lobular carcinoma OR 95% CI	Mastocytosis OR 95% CI	Mixed type OR 95% CI
Age group (ref:20-34)	1-	1-	1-
35-49	3.86 (0.36 7.14)	0.02 (-0.25 2.76)	0.62 (-0.73 9.11)
50-69	0.24 (0.23 1.66)	0.79 (-0.75 23.67)	0.83 (-2.70 15.42)
70+	4.22 (-1.05 16.61)	0.06 (0.03 8.48)	0.61 (-0.49 4.16)
Education (ref: primary)	1-	1-	1-
At least high school	6.69 (-0.14 7.84)	10.38 (2.53 17.54)	4.26 (-1.57 11.67)
Occupation (ref: employed)	1-	1-	1-
Unemployed	2.44 (1.45 5.30)	3.55 (1.50 17.33)	1.51 (-0.72 3.80)
Religion (ref: Muslim)	1-	1-	1-
Christian	0.15 (0.14 4.49)	2.59 (-0.12 3.13)	6.49 (2.16 10.32)

Table 3: Bayesian multinomial model estimates of risk factors associated with histologic type of breast cancer

Variables	Lobular carcinoma OR 95% CI	Mastocytosis OR 95% CI	Mixed type OR 95% CI
Age group (ref:20-34)	1-	1-	1-
35-49	1.03 (0.94 5.44)	1.30 (-2.16 4.83)	0.32 (-3.42 1.07)
50-69	3.10 (0.29 6.85)	0.92 (-4.52 3.94)	0.65 (-3.28 2.39)
70+	0.83 (-0.64 13.29)	0.57 (-0.56 1.20)	0.19 (-8.14 4.99)
Education (ref: primary)	1-	1-	1-
At least high school	1.17 (-1.52 2.84)	1.51 (1.32 8.31)	0.05 (0.01 5.05)
Occupation (ref: employed)	1-	1-	1-
Unemployed	4.5 (0.52 50.20)	3.2 (2.01 11.08)	2.08 (-1.33 4.67)
Religion (ref: Muslim)			
Christian	0.68 (0.30 2.28)	0.54 (0.10 0.82)	0.01 (-6.31 2.37)

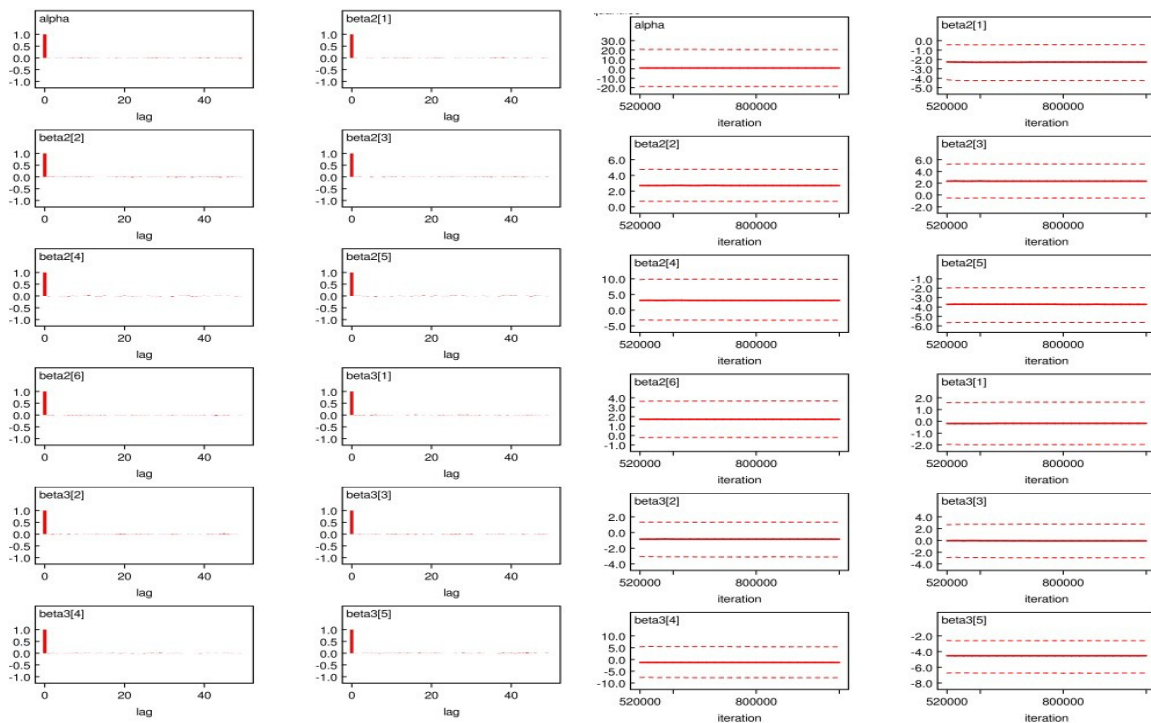


Fig. 1: Win BUGS' output auto-correlation

(OR = 4.5, Cred.I: 0.52-50.20) and mastocytosis (OR = 3.2, Cred.I: 2.01-11.08) form of histologic type compared to those who are either employed by government or private sectors (Table 3).

Once the results of the model are computed, it is important to check for the convergence of Markov Chain Monte Carlo^{22,23}. Figure 1 illustrates the convergence of the Bayesian with non-informative prior using the Gelman-Rubin

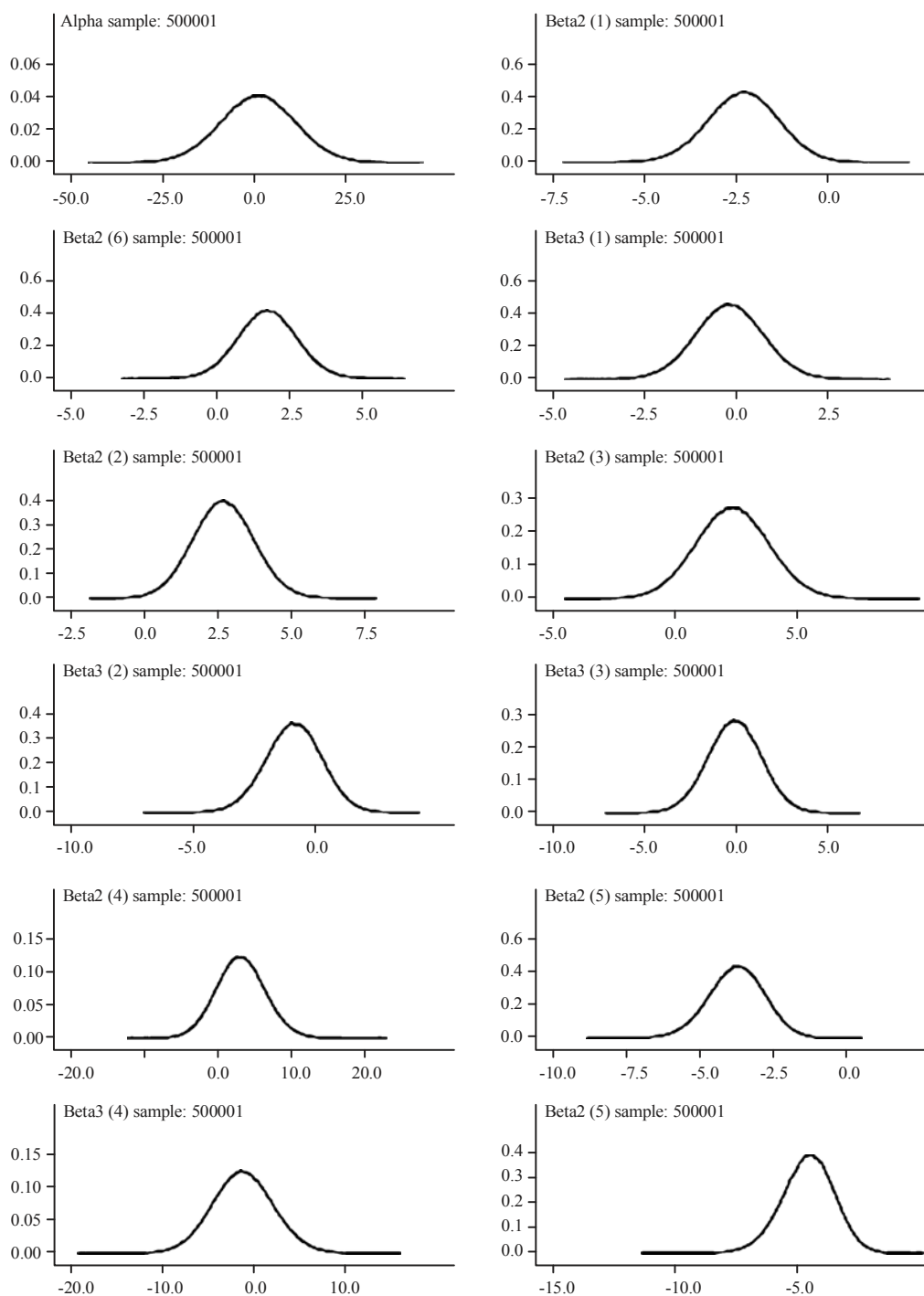


Fig. 2: Win BUGS' output posterior density

Convergence Diagnostic test. The algorithm converged after 1500, 000 iterations. To remove the auto-correlation and burning periods, a lag of 20 was considered and the first 500, 000 iterations removed. The graph shows that all the models were converged. Also, the red lines which represent the within sample variance and the pooled posterior variance

are stationary. Thus, the Gelman-Rubin Convergence Diagnostic test suggests that the algorithm converges.

Figure 2 provides a graphical representation of the posterior density estimate for each parameter. This plot indicates normality for the posterior distribution of each parameter associated in the model.

DISCUSSION

This study examined the relationship between some socio-demographic and medical factors and histologic type of breast cancer at two different hospitals in western Nigeria. The findings showed that 81% women were diagnosed with malignant breast lesion. The study identified age as the only risk factors for women with lobular carcinoma. In contrast, tertiary educational level was found to be associated with breast cancer patient having mastocytosis. Also, the type of occupation had a significant influence on both lobular carcinoma and mastocytosis. Classical approach showed that patient with tertiary educational level was the strongest risk factor for mastocytosis (OR = 10.38) in this part of Nigeria.

The key strength of study was that the data used to ascertain the study outcomes is recent. In addition, the mean age at breast cancer diagnosis was similar to that reported by other studies conducted across Nigeria²⁴⁻²⁸ and rest of the world²⁹⁻³¹. Level of education was also found to be associated with histologic type of breast cancer in our study. Women with tertiary education had significantly higher odds of lobular carcinoma than women with lower educational status. This form of histologic type might have resulted from their exposure to advancement in life like nature of occupation, diet, without observing caution to health management. But there was a lower distribution of lobular carcinoma among those who had less than tertiary education. In addition, in the context of Nigeria no much studies have found any association between various forms of histologic type and education in relation to breast cancer. Therefore, this finding has important implication on the prevention strategies for breast cancer treatment and management among western women of Nigeria. Occupation status is an important factor identified in this study in both classical and Bayesian, this may be related to the level of education status in this part of Nigeria. The odd of getting lobular carcinoma in unemployed women is higher by more than fourth folds (OR = 4.5, Cred.I: 0.52-50.20) compared to employed women in either government or private sectors. Previous studies within the context of Nigeria found that there is an association between occupation and breast cancer risk^{25,27}.

Although this study did not investigate the risk factors for breast cancer in association with its sub molecular types, a recent study conducted by Gordovil-Merino *et al.*³² and Mabula *et al.*²⁷ evaluated the association between SES and breast cancer subtypes using a valid measure of SES and the Surveillance, Epidemiology and End Results (SEER) database. Socio-economic status based on measures of income, occupational class, education and house value were

categorized into quintiles and explored. Their findings showed that a positive association between SES and breast cancer incidence is primarily driven by hormone receptor positive lesion. Malignant breast lesions which can be sub-divided into non-invasive and invasive tumors are documented to be more commonly diagnosed in postmenopausal women³³. A molecular classification of breast cancer, with more than five reproducible subtypes (basal-like, ERBB2, normal-like, luminal A and luminal B) has been defined through gene expression profiling and microarray analysis¹⁵.

Moreover, the results of this suggest that there is a significant difference between the three approaches. The model with histologic type as the outcome variable and age, educational status, religion affiliation and occupation as the covariates was estimated for both the Bayesian, classical and bootstrapping multinomial logistic regression model. A comparison between the three approaches to better apprehend the socio-economic determinants of breast cancer highlights lower standard errors of the estimated coefficients in the Bayesian multinomial logistic regression model. Thus, the Bayesian multinomial logistic regression is more stable. On the other hand, the results from Bayesian approach and classical statistics are difficult to compare because both utilized different tools for decision-making. In addition, when both approaches produce similar results, findings from Bayesian model are given preference because the technique is more robust and precise than the classical statistics. Our results also give some support to previous findings³¹. Addition of priors will actually reduce the variance of the model and thereby lead to a better model in the Bayesian approach. Based on the prior definition and the result from our analysis we concluded that Bayesian approach give better result compared to other techniques utilized in this study and this observation is supported by previous studies.

CONCLUSION

The findings of this study affirm that histologic type is significantly associated with age, educational status religion affiliation and occupation in patient with breast cancer. Also, the study has provided essential information about the prevalence of breast cancer in this part of Nigeria which may explain the reason for modality treatment. Outcome of this paper contribute in a better understanding of association between histologic type and risk factors of breast cancer in Nigeria. Finally, the study demonstrates that Bayesian model performs better than the classical model in apprehending the association between histologic type and risk factors of breast cancer in western Nigeria. In addition, the implication for

research using the Bayesian approach is that even with limited and incomplete data, Bayesian based analysis can produce accurate, reliable inferences to support decisions regarding policies and interventions.

SIGNIFICANCE STATEMENT

The study affirmed a strong association between histologic type, age, educational status religion and occupation in the population. This study discovered that age and educational status had greater influence on all the various histologic type compared in the present study and as such they are more important in assessing risk for histologic type of breast cancer in western Nigeria, particularly for breast cancer among women. Although many pieces of research have been carried out on this subject, this paper steps further by inculcating past knowledge into the model, using Bayesian approach with non-informative prior. The implication for research using the Bayesian approach is that even with limited and incomplete data, Bayesian-based technique can produce accurate, reliable inferences to support decisions regarding policies, interventions and funding priorities compared to classical statistics.

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