

Pre-existing morbidity profile of women newly diagnosed with breast cancer in sub-Saharan Africa: African Breast Cancer—Disparities in Outcomes (ABC-DO) study

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/ijc.33387

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ABSTRACT

The presence of pre-existing morbidities poses a challenge to cancer patient care. There is little information on the profile and prevalence of multi-morbidities in breast cancer patients across middle to lower income countries (MIC and LIC) in Sub-Saharan Africa (SSA). The African Breast Cancer–Disparities in Outcomes breast cancer cohort spans upper MICs South Africa and Namibia, lower MICs Zambia and Nigeria and LIC Uganda. At cancer diagnosis 7 morbidities were assessed: obesity, hypertension, diabetes, asthma/chronic obstructive pulmonary disease, heart disease, tuberculosis and HIV. Logistic regression models were used to assess determinants of morbidities and the influence of morbidities on advanced stage (stage III/IV) breast cancer diagnosis. Among 2189 women, morbidity prevalence was highest for obesity (35%, country-specific range 15-57%), hypertension (32%, 15-51%) and HIV (16%, 2-26%) then for diabetes (7%, 4-10%), asthma (4%, 2-10%), tuberculosis (4%, 0-8%) and heart disease (3%, 1-7%). Obesity and hypertension were more common in upper MICs and in higher socio-economic groups. Overall, 27% of women had at least 2 pre-existing morbidities. Older women were more likely to have obesity (odds ratio: 1.09 per 10 years, 95% CI 1.01-1.18), hypertension (1.98, 1.81-2.17), diabetes (1.51, 1.32-1.74) and heart disease (1.69, 1.37-2.09)

and were less likely to be HIV positive (0.64, 0.58-0.71). Multi-morbidity was not associated with stage-at-diagnosis, with the exception of earlier stage in obese and hypertensive women. Breast cancer patients in higher income countries and higher social groups in SSA face the additional burden of pre-existing non-communicable diseases, particularly obesity and hypertension, exacerbated by HIV in Southern/Eastern Africa.

Keywords: Breast cancer, chronic condition, multi-morbidity, stage at diagnosis and sub-Saharan Africa

List of abbreviations

ABC-DO	Africa breast Cancer Disparity in Outcomes
BMI	Body mass index
CD	Communicable diseases
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
ELISA	Enzyme-linked immunosorbent assay
HICs	High income countries
HIV	Human immunodeficiency virus
LMICs	Low and middle income countries
NCDs	Non-Communicable diseases
OR	Odds ratio
SD	Standard deviation
SEP	Socio-economic position
SSA	Sub-Saharan Africa
TNM	Tumour, node, metastasis classification

Novelty and impact statement

“Pre-existing morbidities in women with breast cancer poses a challenge to patient care. This study shows the prevalence and patterns of chronic conditions and multi-morbidity in women newly diagnosed with breast cancer in five SSA countries in different stages of economic, developmental and lifestyle transition. Obesity and hypertension are more common in higher social groups and associated with early stage breast cancer diagnosis. The burden of pre-existing multi-morbidities among breast cancer patients in SSA is substantial and is exacerbated by HIV”

INTRODUCTION

Breast cancer is the most common malignancy and the leading cause of cancer mortality in women worldwide. It is also the most common cancer among women in sub-Saharan Africa (SSA)¹ where the incidence of this cancer is on the rise. These temporal changes form part of an epidemiological transition occurring in SSA, characterized by improved control of infectious diseases, ageing populations and increasing prevalence of risk factors for non-communicable diseases (NCD) due to economic advancement, urbanisation and lifestyle modifications.² These syndemics also result in multi-morbidity (the co-occurrence of two or more chronic comorbidities in one person)³ at the individual level, including in breast cancer patients.

Survival after breast cancer diagnosis is determined by patient characteristics and disease-related factors such as stage at diagnosis and breast cancer subtypes.⁴ In addition to these factors, studies mostly originating from high-income countries (HICs) have shown that several pre-existing morbidities are associated with lower breast cancer survival, poorer overall outcomes and they also impact on treatment recommendations and tolerance.^{5, 6} These morbidities include obesity, diabetes and insulin resistance, stroke, body composition and mental health illnesses, i.e. conditions which tend to be more common in older breast cancer patients.⁷

Pre-existing chronic conditions have also been linked to stage at cancer diagnosis, but the direction, degree and mechanisms of associations have not been consistent.⁸⁻¹⁰ The presence of pre-existing morbidities have been linked to increased risk of metastatic disease at diagnosis⁸, whereas links to earlier stage at diagnosis have been reported in settings served by population-based breast cancer screening.¹¹ Some studies also noted earlier stage at diagnosis in women with hypertension^{9, 12}, possibly arising from a 'surveillance effect' (i.e. greater clinical scrutiny upon follow-up for hypertension/ greater opportunity to seek help during health system contacts for other illnesses).

In the SSA setting, there is a paucity of data on the profile of pre-existing morbidity profiles among breast cancer patients. Such profiles are likely to differ across SSA countries at differing stages of economic, developmental and lifestyle transitions, i.e. different in SSA middle income countries (MICs) from low income countries (LICs).^{13, 14} Further, in addition to the aforementioned conditions, the setting-pertinent infectious disease of HIV needs to be taken into account, due to the ageing HIV-positive population successfully treated with antiretroviral

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drugs.¹⁵ Establishing these SSA-specific morbidity profiles of breast cancer patients will form a first step to inform priorities for feasible management strategies in constrained public health systems.

To date, we have investigated this morbidity profile among breast cancer patients diagnosed at five hospitals in South Africa and found that 44% of women had pre-existing morbidities at diagnosis: 53% were obese, 41% hypertensive, 22% HIV-positive and 14% were diabetic. Multi-morbidities were linked to older age and higher socioeconomic status.¹² In the present study, we broadened our perspective to five SSA countries, including the upper MICs of South Africa and Namibia, lower MICs of Zambia and Nigeria and LIC of Uganda. Our aims were three-fold: (i) to describe the prevalence and profile of pre-existing chronic conditions and multi-morbidity (at least two chronic conditions in addition to breast cancer) in women newly diagnosed with breast cancer in 5 countries in SSA; (ii) to determine the socio-demographic factors associated with individual chronic conditions and multimorbidity and (iii) to assess whether any of the individual chronic conditions or multimorbidity was associated with breast cancer stage at diagnosis.

METHODS

Study design and study setting

Presence of pre-existing chronic conditions and multi-morbidity in women newly diagnosed with breast cancer was examined within the African Breast Cancer-Disparities in Outcomes study (ABC-DO) cohort, a prospective multi-country hospital based breast cancer cohort in Southern (South Africa, Namibia and Zambia), Western (Nigeria) and Eastern (Uganda) SSA

countries.¹⁶ Incident breast cancer patients were recruited at Windhoek Central Hospital, Namibia; Abia State University Teaching Hospital and the Maranatha private clinic, Aba and the Federal Medical Centre, Owerri, Nigeria; Chris Hani Baragwanath Academic hospital, Soweto, South Africa; Mulago Hospital and the Uganda Cancer Institute, Kampala, Uganda; and the Cancer Diseases Hospital and University Teaching Hospital, Lusaka, Zambia. The ABC-DO protocol was previously published.¹⁶

Participants

Recruitment commenced from September through December 2014 in most centres and was completed by April 2017 except in Zambia (May 2016 through September 2017). Women ≥ 18 years of age with a clinically/histologically confirmed newly diagnosed breast cancer who provided written consent to participate in the study, and provided access to their medical records and tumour tissue were enrolled. ABC-DO was approved by ethics committees at each recruitment institution: IARC (IEC 13–19, IEC15–18), the London School of Hygiene and Tropical Medicine (6459), University of Witwatersrand, South Africa (M150345), Council for Science and Technology (HS 1588) and the Ministry of Health and Social Services of Namibia (17/3/3), University of Zambia Biomedical Research Ethics Committee (004-08-15), Federal Medical Centre Owerri, Abia State University Teaching Hospital and Uganda National Council for Science and Technology (HS 1588). This study was performed in accordance with the Declaration of Helsinki.

The present analyses of pre-existing morbidities were conducted overall and by site-race group, with Namibian women separated into black and non-black ethnic groups as these groups were

different in socio-economic profile and stage distribution.¹⁷ Participants from other countries were almost exclusively black women, forty two non-black South Africans were excluded from the analysis as this group was too small to analyse separately.

Exposure and outcome data

The same face-to-face baseline questionnaire was utilized in all hospitals except in South Africa where a pre-existing survey instrument was administered and harmonized to ABC-DO specifications. For this analysis we included questions on age, self-identified ethnic group, and marital status. Educational level was categorised as primary education or none and secondary education or higher. We grouped employment into 2 categories, employed (highly skilled/skilled, employed in South Africa) versus unemployed (unskilled, unemployed and retired in South Africa). A score for socioeconomic position (SEP) was generated from self-reported household facilities and possessions: home ownership, flush toilet, indoor running water, vehicle, electricity, gas or electric stove, refrigerator, landline phone and a bed. A score of +1 was allocated to each possession ranging from 0 (low) to 9 (high).

We examined the presence of seven chronic conditions: obesity, hypertension, diabetes, heart disease, asthma/chronic obstructive pulmonary disease (COPD), HIV infection and tuberculosis. The 7 conditions were included because of their known association with breast cancer prognosis (obesity¹⁸, diabetes¹⁹, HIV⁴), their known impact on treatment (e.g. cardiotoxicity and worsening of hypertension²⁰) and/or their known high prevalence in the least parts of SSA where regular treatment may provide an avenue for early cancer detection (e.g. HIV and tuberculosis²¹, COPD²², hypertension and heart disease²³). Body weight and height

were measured at enrolment, and obesity was defined as a body mass index (BMI) ≥ 30.0 kg/m². Patients were asked if they had ever been treated for tuberculosis and whether they had ever been diagnosed and treated with hypertension, diabetes, heart disease, asthma/COPD (Questionnaire on chronic conditions collected provided as supplementary material, page 5). HIV infection (yes vs. no/not known) was based on self-reports, with 90% of the cohort (apart from South Africa) reporting the later, however there was a 97% agreement with clinical records among those reported negative. In South Africa HIV status was tested as part of the diagnostic workup, using the enzyme-linked immunosorbent assay by the National Health Laboratory Services. We defined multi-morbidity as having ≥ 2 of these seven chronic conditions, in addition to breast cancer.

Breast cancer stage at diagnosis was determined using the American Joint Committee on Cancer (AJCC) TNM staging system²⁴ and categorized for analyses as early (stages I & II) and advanced (stages III & IV).

Statistical methods

We described the pattern and prevalence of each chronic condition by site-race group using Pearson's chi squared and Fishers Exact tests. We examined associations of socio-demographic factors with each chronic condition and with multi-morbidity (≥ 2 of these chronic conditions in addition to the breast cancer) using logistic regression analysis. Logistic regression was also used to examine whether each chronic condition and multi-morbidity were associated with advanced stage breast cancer (stages III & IV), as compared to early stage breast cancer (stages I & II). Variables for which p values were < 0.1 in bivariate analysis with advanced stage breast

cancer were evaluated and ORs were assessed adjusting for each covariate, HIV status, age, and country (as a proxy for level of health care). Analysis was performed using Stata version 15 (StataCorp Ltd, Texas, USA).

RESULTS

A total of 2189 women were included: 720 (33%) from South Africa, 478 (22%) (99 non-black and 379 black) from Namibia, 187 (9%) from Zambia, 382 (17%) from Nigeria and 422 (19%) from Uganda (Table 1). The mean age at diagnosis was 51.7 ± 13.9 , with women from Zambia, Nigeria and Uganda (range of mean age 48.4 – 49.4 years) significantly younger than women from Namibia and South Africa (range of mean age 52.5 - 57.1 years). Overall 62% of the women had at least secondary school education with the non-black Namibian (87%), South African (77%) and Nigerian (72%) women more likely to have had at least secondary education compared to black Namibian (49%), Zambian (47%) and Ugandan (42%) women. In keeping with these low and middle income (LMIC) settings, most women had low to medium SEP with higher SEP in non-black Namibia women. Smoking prevalence was low, ranging from < 1% in Nigeria to 43% among the non-black Namibian women. Approximately 59% of the women presented with advanced stage breast cancer overall (50% in South Africa to 75% in Nigeria), with the exception of non-black Namibian women where the majority presented with early stage disease (78%) (Table1).

Prevalence of chronic conditions and multi-morbidity

Hypertension and obesity dominated as the most common chronic conditions in breast cancer patients in each country, with hypertension ranking first in all countries except in South Africa where obesity ranked as the most common pre-existing chronic condition. HIV ranked 3rd prevalent in all countries except in non-black Namibians (where asthma/COPD was in 3rd rank) and in Nigeria (diabetes ranked 3rd). Diabetes was the fourth most prevalent chronic condition in most countries except among the black Namibian women (tuberculosis was 4th) and in Nigeria (heart disease was 4th) (Table 2). Overall South Africa had the highest prevalence of HIV in the whole cohort (26%) (Table 2) with 42% of the women <50 years of age infected with HIV (Figure 1).

Twenty seven percent of the women newly diagnosed with breast cancer presented with multi-morbidity (presence of ≥ 2 additional chronic conditions) ranging from 42% in South Africa to 11% in Uganda (Table 2). Percentages of women with multi-morbidity was highest in South African women both under and over age 50, with 49% of the women ≥ 50 years presenting with multi-morbidity in addition to breast cancer. Women from lower MICs Zambia and Nigeria and LIC Uganda had the least prevalence of multi-morbidity in both age groups (Figure 1).

With 7 conditions included, of a possible 128 (2^7) morbidity combinations, 57 combinations were present among the 2189 women and only 16 combinations were present in at least 5 women. The profile and prevalence of these combinations for the 11 most common combinations in each population group is shown in Figure 2 (i.e. no pre-existing morbidities and ten combinations with at least one pre-existing morbidities). Where multi-morbidity was present, obesity and hypertension was the dominant combination, affecting 15% of Namibian

non-black and 14% of South African women. The only other combination affecting at least 5% of breast cancer patients in a given group was obesity and HIV in South Africa.

Determinants of chronic conditions

Associations of socio-demographic factors with each chronic condition are presented in table 3. In the mutually adjusted analysis of all countries combined, older women were significantly more likely to be obese, hypertensive, diabetic and have heart disease and less likely to be living with HIV. Of the three measures of socio-economic status, SEP was most frequently associated with the presence of a chronic condition. Women with higher SEP (7-9 (high) and 4-6 (medium)) were more likely to be obese and diabetic compared with women with low SEP (0-3). High SEP women were also more likely to have hypertension compared to those with low SEP (OR: 1.89, 95% CI 1.33-2.59). Associations of age and SEP with the two communicable diseases, tuberculosis and HIV, tended to be in the opposite direction to those for the aforementioned NCDs. Notably, women with medium SEP were less likely to have HIV compared to the women with low SEP. Those employed were more likely to be obese while level of education was not significantly associated with any chronic condition except in Nigeria where those with secondary education and above were more likely to have heart disease (result not shown).

Determinants of the presence of pre-existing multi-morbidities mirror the associations above, particularly for the NCDs, as the co-presence of obesity and hypertension was the most prevalent combinations. Adjusting for age and country site higher SEP compared to low SEP

was associated with greater risk for multi-morbidity at breast cancer diagnosis (Supplementary table 1).

Influence of pre-existing morbidities on stage at diagnosis

Among 2066 women with known stage at diagnosis, investigations of whether pre-existing morbidities affected stage at diagnosis are illustrated in Figure 3 for each site, and results of the ABC-DO wide pooled analysis are shown in table 4 and supplementary table 2. Most site-specific associations were not significant or suggestive, with the following exceptions. Adjusting for age at diagnosis, obese women from Zambia (OR: 0.36, 95% CI 0.16-0.78) and hypertensive women from Nigeria (OR: 0.57, 95% CI 0.33-0.98) were less likely to be diagnosed with advanced stage breast cancer compared to their country-counterparts without these conditions. In contrast, among South African women, those women who had tuberculosis were more likely to be diagnosed with advanced stage breast cancer than those without such a history (OR: 1.91, 95% CI 1.02-3.57). Nigeria, Zambian and Ugandan women who were HIV infected were more likely to be diagnosed with advanced stage breast cancer than their HIV-negative counterparts, though these associations were not significant and were not present in all settings (Figure 3).

Thus meta-analytic estimates across all population groups suggested no association of tuberculosis, asthma/COPD, diabetes and HIV with stage at diagnosis, consistent with the pooled analyses in Table 4. However for hypertension, in meta-analyses, there was a suggestion of a 17% (-3% to 33%) relative reduction in advanced stage breast cancer associated with having this condition, which increased to a 35% (1 to 55%) reduction in pooled analyses

adjusted for HIV. Similarly for obesity, the meta-analysis was suggestive of 12% (95% CI -8% to 28%) reduced odds of advanced stage at diagnosis, which became significant in pooled analyses (28% reduction (1 to 48%). Despite these individual conditions of obesity and hypertension being the most common multi-morbidity combination, the overall effect of multi-morbidity on advanced stage at cancer diagnosis was borderline suggestive of a positive association (OR: 1.34, 95% CI 0.95-1.89) (Table 4).

Discussion

Summary of findings

In this large cohort of breast cancer patients in five SSA countries, the prevalence of at least one of seven pre-existing chronic conditions (obesity, hypertension, diabetes, heart disease, asthma/COPD, HIV infection and tuberculosis) was high (65%) and 27% of women had at least two pre-existing chronic conditions (multi-morbidity). Obesity and hypertension were the two most frequent conditions present, both individually and as a combination amongst women with multi-morbidities, particularly affecting older women and groups with higher socioeconomic status both at the intra-country individual level and, reflecting epidemiologic transitions, at national levels. HIV ranked 3rd in most countries except in non-black Namibian women and in West African Nigeria. The management of breast cancer in SSA thus needs to consider this high percentage of NCDs, alone or in combination with HIV. Nevertheless, none of the seven chronic conditions investigated were positively associated with having advanced stage breast cancer at diagnosis, with the exception of obesity and hypertension which was associated with having early stage breast cancer. The latter findings points to an opportunity to

further increase early diagnosis, in an attempt to counterbalance any survival disadvantage among these women.

Major prevalent chronic conditions: in the population as risk factors for breast cancer and impact on prognosis

Multi-morbidity prevalence closely tracked the wealth index of the countries under investigation and the socioeconomic position scores of the women under investigation. Women from higher MICs with more advanced westernised lifestyle transitions had the greater multi-morbidity burden (South Africa (42%) followed by Namibia) than those from lower middle income Zambia and Nigeria and low income Uganda. These findings were in keeping with ranges of 14% to 68% reported from other studies.^{12, 25, 26} With 27% of our patients presenting with multi-morbidity (≥ 2 chronic conditions), SSA is facing a significant challenge of multi-morbidity comprising both infectious diseases combined with the rapidly growing NCD prevalence as countries transition to westernized lifestyles. Hypertension ranked as the most common chronic condition in most countries except in South Africa where obesity ranked first, ranging from 15% in LIC Uganda to 51% amongst MIC non-black Namibian women. Hypertension is a public health challenge in Africa with 46% of its population aged 25 years and over living with hypertension.²⁷ Hypertension might be positively linked to risk of breast cancer especially in postmenopausal women²⁸ hence its high prevalence among our women is particularly worrying. More critically, during the therapeutic phase, chemotherapy can worsen hypertension and cause cardiomyopathy.²⁹

Obesity, a known risk factor for breast cancer in postmenopausal women,³⁰ has also been associated with worse breast cancer outcomes for women of all ages.¹⁸ Obesity was commonly reported in this study though with high variation across countries in various stages of lifestyle transition. South Africa has the highest prevalence with 57% of the women obese while Uganda had the lowest prevalence (15%). The emerging prevalence of obesity in SSA has been largely attributed to the rising empowerment of women, sedentary lifestyles, economic development and urbanization³¹ ultimately leading to nutritional transition. Obesity at postmenopausal ages is a driver of increasing breast cancer incidence rates, thus in this instance the rising obesity rates are fuelling more cases with poorer prognosis. Diabetes with prevalence ranging from 4% in Uganda to 10% in South Africa is also a known risk factor for breast cancer in postmenopausal women,³² it is also associated with worse survival with up to an increased risk of 52% in overall mortality.³³

The high burden of HIV amongst particularly our southern African women in this study is of continued concern with HIV now regarded as a chronic infectious disease, though the general consensus is that there is no significant link between HIV and risk of breast cancer;³⁴ however, studies have reported poorer prognosis in HIV positive patients with breast cancer.^{4, 35}

Determinants of chronic conditions

As expected, most chronic conditions were more prevalent in older women, a finding consistent with previous studies in SSA.^{12, 36} We also found that women with higher SEP were more likely to present with obesity, hypertension and diabetes in contrast to findings from other mainly HIC studies where multimorbidity was more prevalent at lower SEP.^{26, 37, 38} However our

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findings were consistent with other studies from LMICs for multimorbidity,²⁵ overweight/obesity, hypertension and diabetes.³⁶ These findings perhaps reflects westernized lifestyle and dietary transitions first affecting higher SEP groups with the capital needed to purchase and live modern lifestyles.³⁹

Impact on stage

It is known that advanced cancer stage at diagnosis is affected by chronic conditions,⁸⁻¹⁰ however some studies have consistently demonstrated earlier stage at diagnosis with chronic conditions.^{11, 12, 40} In this study we found no significant association between multi-morbidity and advanced stage at breast cancer diagnosis. Women who had hypertension at diagnosis of breast cancer were more likely to have early stage breast cancer, perhaps due to their regular access to the health system facilities for other conditions.^{36, 37} Our patients that were obese were less likely to present with advanced stage breast cancer, this is in contrast to studies suggesting that higher BMI is associated with a more advanced stage of breast cancer at diagnosis.^{41, 42} Our finding could be attributable to reverse causality given the 59% of late stage tumour in the cohort.

Strengths and limitations

This study benefitted from a diversity of countries across SSA, a wide range of morbidities included, a strong SSA-perspective on the selection of morbidities, heterogeneity in socio-demographic factors, measured BMI, tested HIV in South Africa and a prospective design. However, the sample was tertiary hospital-based patients, and many breast cancer patients in SSA may never reach this level of the health system. Further limitations were noted: most of

these chronic conditions were self-reported, hence we could have underestimated the prevalence of multi-morbidity especially in women with lower SEP. In SSA, low socioeconomic status is associated with lower access to care and treatment⁴³ and thus there could be lower rates of diagnosis of these chronic conditions in women with lower SEP.

Implications on therapeutic management

The implication of multi-morbidity in women with breast cancer is profound including the high cost of care⁴⁴ and poor quality of life⁴⁵. Breast cancer patients with multi-morbidity are less likely to receive surgery,⁴⁶ less likely to receive adjuvant chemotherapy,⁴⁷ more likely to receive a reduced dose and less likely to complete chemotherapy treatment when initiated,⁴⁸ and less likely to initiate timely radiotherapy after surgical treatment.⁴⁹ Multi-morbidity may cause higher rates of adverse effects of treatment⁵⁰ affecting overall goal of care. It has been associated with an increased risk of cardiotoxicity, immunosuppression during chemotherapy and radiotherapy for HIV positive women.⁵¹ Further, at the health system level, the management of multi-morbidity is much more complicated and demanding for the patients and the health system, requiring an integrated approach and long-term care.⁵² To effectively address these changing needs, countries in SSA require detailed surveillance on chronic condition trends to assist in developing models of care appropriate for LMICs.

Conclusion

There is a high prevalence of chronic conditions and multi-morbidity in our breast cancer patients and socio-demographic factors play a major role in its determinants in SSA. With increasing life expectancy, the rapidly increasing multi-morbidity burden in SSA is of great

concern for its under resourced health care services. SSA studies of the impact of these morbidities on survival and therapeutic management are needed.

DECLARATIONS

Ethics statement: ABC-DO was approved by ethics committees at each recruitment institution: IARC (IEC 13–19, IEC15–18), the London School of Hygiene and Tropical Medicine (6459), University of Witwatersrand, South Africa (M150345), Council for Science and Technology (HS 1588) and the Ministry of Health and Social Services of Namibia (17/3/3), University of Zambia Biomedical Research Ethics Committee (004-08-15), Federal Medical Centre Owerri, Abia State University Teaching Hospital and Uganda National Council for Science and Technology (HS 1588). All participants provided written informed consent.

Data availability statement: Data for this study contain confidential patient information. The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no conflict of interest

Grant: Susan G. Komen for the Cure Foundation; Grant number: IIR 13264158; Grant sponsor: IARC.

Funding: ABC-DO was supported by IARC, Susan. G. Komen (IIR 13264158, GSP18IARC001, GSP19IARC001 and as part of “Implementing breast cancer care efficiency in Zambia through specialized health provider training and m-health evaluation of patient

outcomes” for the Zambian site). This work was also supported by (i) NIH grant (NCI 1R01CA192627) <http://grantome.com/grant/NIH/R01-CA192627-01>, and (ii) the Cancer Association of South Africa (CANSA) grant “Down-staging and improving survival of breast cancer in South Africa” <http://www.cansa.org.za/downstaging-and-improving-survival-of-breast-cancerin-sa-dr-herbert-cubasch> (HC). SAN is supported by the DST-NRF Centre of Excellence in Human Development at the University of the Witwatersrand, Johannesburg, South Africa.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The Wits Health Consortium (PTY) Ltd provided support in the form of payroll administration of salaries from grant funds for authors OA, MJ, SAN, but did not have any additional role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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All authors contributed to the interpretation of the results and critically reviewed the first draft of the manuscript; they all read and approved the final version of the manuscript, and they all agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgements:

The authors thank the women who participated in this study. They also thank the dedicated team of study research assistants for their help and assistance with the study.

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Figure 1: The prevalence of pre-existing chronic conditions at breast cancer diagnosis in the ABC-DO study, overall and by age at cancer diagnosis. Multimorbidity prevalence indicates the presence of two or more of the seven pre-existing chronic condition at the time of breast cancer diagnosis.

Figure 2: Profile of the combination of seven pre-existing morbidities amongst breast cancer patients in the ABC-DO study.

Figure 3: Odds ratios of women being diagnosed with advanced stage breast cancer (stages III & IV) associated with each of the seven chronic conditions examined, by sub-Saharan Africa countries in the ABC-DO study.

Table 1: Characteristics of women newly diagnosed with breast cancer in Sub-Saharan Africa, by country and race; ABC-DO study.

	Southern Africa (S.A.)				West Africa	East Africa	Total
	South Africa	Namibia Non-Black	Namibia Black	Zambia	Nigeria	Uganda	
	N=720 (%)	N=99 (%)	N=379 (%)	N=187 (%)	N=382 (%)	N=422 (%)	N=2189 (%)
Age in years, mean ± SD	54.5±14.3	57.1±12.4	52.5±14.6	49.4±14.2	48.8±12.2	48.4±12.6	51.7±13.9
BMI (kg/m²)	31.7±7.7	29.1±6.8	26.4±6.7	26.5±6.3	26.4±5.7	25.6±4.6	28.1±7.0
Marital status							
Married	233 (32.4)	58 (58.6)	122 (32.2)	110 (58.8)	250 (65.4)	199 (47.2)	972 (44.4)
Not married	487 (67.6)	41 (41.4)	257 (67.8)	77 (41.2)	132 (34.6)	223 (52.8)	1217 (55.6)
Received secondary education							
Yes	551 (76.5)	86 (86.9)	184 (48.5)	87 (46.5)	276 (72.3)	178 (42.2)	1362 (62.2)
No	169 (23.5)	13 (13.1)	195 (51.5)	100 (53.5)	106 (27.7)	244 (57.8)	827 (37.8)
Employment status							
Employed	202 (28.1)	98 (99.0)	346 (91.3)	73 (39.0)	357 (93.5)	331 (78.4)	1407 (64.3)
Unemployed	518 (71.9)	1 (1.0)	33 (8.7)	114 (61.0)	25 (6.5)	91 (21.6)	782 (35.7)
SEP							
Low (0-3)	273 (37.9)	0 (0.0)	166 (43.8)	67 (35.8)	161 (42.1)	249 (59.0)	916 (41.8)
Medium (4-6)	433 (60.1)	39 (39.4)	130 (34.3)	69 (36.9)	167 (43.7)	90 (21.3)	928 (42.4)
High (7-9)	14 (1.9)	60 (60.6)	83 (21.9)	51 (27.3)	54 (14.1)	83 (19.7)	345 (15.8)
Ever consumed alcohol?							
No	565 (78.5)	37 (37.4)	185 (48.8)	123 (65.8)	178 (46.6)	225 (53.3)	1313 (60)
Yes	155 (21.5)	62 (62.6)	194 (51.2)	64 (34.2)	204 (53.4)	197 (46.7)	876 (40)
Ever smoked?							
No	677 (94.0)	56 (56.6)	324 (85.5)	185 (98.9)	381 (99.7)	408 (96.7)	2031 (92.8)
Yes	43 (6.0)	43 (43.4)	55 (14.5)	2 (1.1)	1 (0.3)	14 (3.3)	158 (7.2)
Stage at diagnosis							
Stage I & II	347 (49.6)	77 (77.8)	139 (36.7)	60 (40.3)	88 (25.1)	142 (36.5)	853 (41.3)
Stage III & IV	353 (50.4)	22 (22.2)	240 (63.3)	89 (59.7)	262 (74.9)	247 (63.5)	1213 (58.7)

Missing values for covariates were as follows: Stage at diagnosis (n=132); BMI (Body mass index), SEP (Socio-economic position), SD (standard deviation)

Table 2: Prevalence of pre-existing chronic conditions in women newly diagnosed with breast cancer in Sub-Saharan Africa, by country-site; ABC-DO study.

	Southern Africa (S.A.) Upper MICs			S.A. Lower MIC	West Africa Lower MIC	East Africa LIC	
	South Africa	Namibia Non-Black	Namibia Black	Zambia	Nigeria	Uganda	Total
Ranked chronic conditions	N=720 (%)	N=99 (%)	N=379 (%)	N=187 (%)	N=382 (%)	N=422 (%)	N=2189 (%)
Most common	Obesity (57)	Hypertension (51)	Hypertension (43)	Hypertension (29)	Hypertension (28)	Hypertension (15)	Obesity (35)
2nd most common	Hypertension (38)	Obesity (43)	Obesity (27)	Obesity (24)	Obesity (26)	Obesity (15)	Hypertension (32)
3 rd most common	HIV (26)	Asthma/COPD (10)	HIV (15)	HIV (18)	Diabetes (8)	HIV (13)	HIV (16)
4 th most common	Diabetes (10)	Diabetes (8)	Tuberculosis (8)	Diabetes (4)	Heart disease (5)	Diabetes (4)	Diabetes (7)
5 th most common	Tuberculosis (7)	Heart disease (7)	Asthma/COPD (7)	Asthma/COPD (4)	HIV (3)	Asthma/COPD (2)	Asthma/COPD (4)
6 th most common	Asthma/COPD (4)	HIV (2)	Diabetes (6)	Tuberculosis (3)	Asthma/COPD (3)	Heart disease (2)	Tuberculosis (4)
7 th most common	Heart disease (2)	Tuberculosis (1)	Heart disease (5)	Heart disease (1)	Tuberculosis (0)	Tuberculosis (1)	Heart disease (3)
Chronic conditions	N positive (% positive)						
Obese	410 (56.9)	43 (43.4)	104 (27.4)	45 (24.1)	98 (25.7)	62 (14.7)	762 (34.8)
Hypertension	271 (37.6)	50 (50.5)	161 (42.5)	54 (28.9)	105 (27.5)	63 (14.9)	704 (32.2)
HIV	187 (26)	2 (2.0)	56 (14.8)	34 (18.2)	13 (3.4)	56 (13.3)	348 (15.9)
Diabetes	69 (9.6)	8 (8.1)	21 (5.5)	7 (3.7)	31 (8.1)	17 (4.0)	153 (7.0)
Asthma/COPD	25 (3.5)	10 (10.1)	27 (7.1)	7 (3.7)	11 (2.9)	10 (2.4)	90 (4.1)
Tuberculosis	48 (6.7)	1 (1.0)	29 (7.7)	6 (3.2)	0 (0.0)	3 (0.7)	87 (4.0)
Heart disease	13 (1.8)	7 (7.1)	17 (4.5)	1 (0.5)	18 (4.7)	8 (1.9)	64 (2.9)
Any chronic condition	617 (85.7)	73 (73.7)	256 (67.5)	114 (61)	193 (50.5)	163 (38.6)	1416 (64.7)
Number of pre-existing chronic conditions							
0	103 (14.3)	26 (26.3)	123 (32.5)	73 (39.0)	189 (49.5)	259 (61.4)	773 (35.3)
1	315 (43.8)	37 (37.4)	141 (37.2)	79 (42.2)	130 (34)	115 (27.3)	817 (37.3)
2	210 (29.2)	26 (26.3)	80 (21.1)	31 (16.6)	47 (12.3)	41 (9.7)	435 (19.9)
3	82 (11.4)	8 (8.1)	28 (7.4)	3 (1.6)	12 (3.1)	6 (1.4)	139 (6.3)
4+	10 (1.4)	2 (2.0)	7 (1.8)	1 (0.5)	4 (1.0)	1 (0.2)	25 (1.1)
Multimorbidity (≥2)	302 (41.9)	36 (36.4)	115 (30.3)	35 (18.7)	63 (16.5)	48 (11.4)	599 (27.4)

- MICs (Middle income countries), LIC (Low income countries), COPD (Chronic obstructive pulmonary disease),

Table 3: Associations of socio-demographic characteristics with each chronic conditions, among breast cancer patients in Sub-Saharan Africa, ABC-DO study. ORs are mutually adjusted.

Socio-demographic characteristics	Non-communicable diseases					Communicable diseases		NCDs combined
	Obesity (BMI \geq 30.0 kg/m ²)	Hypertension	Diabetes	Asthma/COPD	Heart disease	HIV positive	Tuberculosis	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (10 year increase)	1.09 (1.01-1.18) ^a	1.98 (1.81-2.17) ^b	1.51 (1.32-1.74) ^b	1.08 (0.91-1.29)	1.69 (1.37-2.09) ^b	0.64 (0.58-0.71) ^b	0.97 (0.81-1.15)	1.62 (1.50-1.76) ^b
Marital status								
Not married	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Married	1.25 (1.02-1.54) ^a	1.07 (0.87-1.33)	1.39 (0.97-2.00)	0.90 (0.57-1.42)	0.80 (0.45-1.43)	0.51 (0.39-0.67) ^b	0.62 (0.36-1.03)	1.02 (0.84-1.25)
Highest level of education								
Primary education and below	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Secondary education and above	1.01 (0.79-1.29)	1.05 (0.82-1.36)	0.77 (0.51-1.16)	1.03 (0.60-1.77)	1.06 (0.56-2.02)	1.18 (0.86-1.61)	1.13 (0.65-1.97)	1.04 (0.82-1.33)
Employment status								
Unemployed	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Employed	1.51 (1.17-1.97) ^a	0.98 (0.74-1.29)	1.11 (0.68-1.82)	1.16 (0.62-2.16)	0.71 (0.32-1.56)	0.88 (0.65-1.18)	0.90 (0.51-1.59)	1.22 (0.95-1.58)
SEP								
Low (0-3)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Medium (4-6)	1.93 (1.54-2.40) ^b	1.20 (0.95-1.51)	1.77 (1.16-2.69) ^a	1.85 (1.09-3.15) ^a	1.08 (0.58-1.99)	0.60 (0.46-0.79) ^b	1.35 (0.83-2.20)	1.76 (1.42-2.18) ^b
High (7-9)	3.05 (2.22-4.18) ^b	1.86 (1.33-2.59) ^b	3.25 (1.88-5.62) ^b	1.74 (0.86-3.51)	1.59 (0.72-3.52)	0.65 (0.41-1.02)	1.26 (0.55-2.86)	2.75 (2.02-3.75) ^b
Country								
Uganda	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Namibia Black	1.93 (1.34-2.78) ^b	3.76 (2.61-5.41) ^b	1.06 (0.54-2.09)	2.71 (1.28-5.76) ^a	1.84 (0.76-4.45)	1.27 (0.84-1.94)	10.61(3.18-35.46) ^b	2.60 (1.90-3.56) ^b
Namibia Non-Black	2.26 (1.35-3.77) ^a	2.98 (1.73-5.12) ^b	0.89 (0.35-2.27)	3.11 (1.17-8.29) ^b	2.30 (0.71-7.46)	0.25 (0.10-1.07)	1.30 (0.13-13.08)	2.94 (1.72-5.01) ^b
Nigeria	1.73 (1.19-2.51) ^a	2.26 (1.54-3.32) ^b	1.98 (1.04-3.76) ^a	1.09 (0.44-2.66)	2.82 (1.15-6.90) ^a	0.27 (0.14-0.50) ^b	Omitted	2.23 (1.62-3.08) ^b
South Africa	9.68 (6.65-14.07) ^b	2.67 (1.82-3.92) ^b	2.32 (1.19-4.55) ^a	1.29 (0.54-3.06)	0.53 (0.18-1.57)	2.72 (1.82-4.08) ^b	8.10 (2.33-28.12) ^a	6.13 (4.40-8.54) ^b
Zambia	1.77 (1.12-2.78) ^a	2.11 (1.33-3.33) ^a	0.76 (0.30-1.91)	1.49 (0.54-4.10)	0.22 (0.03-1.79)	1.75 (1.06-2.90) ^a	4.38 (1.06-18.15) ^a	1.93 (1.30-2.86) ^a

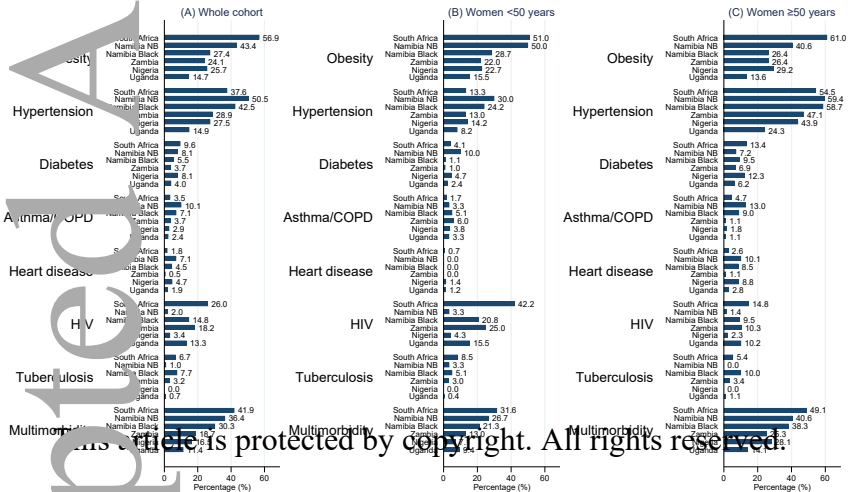
BMI (Body mass index), OR (Odds ratio), 95% CI (95% confidence interval), SEP (Socio-economic position), COPD (Chronic obstructive pulmonary disease), NCDs (Non-communicable diseases), NCDs (Obesity, hypertension, diabetes, asthma/COPD, heart disease), ^a Significant at p<0.05, ^b Significant at p<0.00

Table 4: Multiple logistic regression models of chronic conditions and presence of multimorbidity (≥ 2 chronic conditions) as predictors of advanced stage breast cancer (stages III & IV) in women newly diagnosed with breast cancer in Sub-Saharan Africa, ABC-DO study.

Chronic conditions	Odds ratio	95% CI	P value
Obese			
No	1.00	Reference	0.049
Yes	0.72	0.52-0.99	
Hypertension			
No	1.00	Reference	0.015
Yes	0.65	0.45-0.92	
HIV			
Negative	1.00	Reference	0.331
Positive	0.85	0.58-1.22	
Any chronic condition			
No	1.00	Reference	0.120
Yes	1.30	0.92-1.84	
Multimorbidity			
< 2 chronic conditions	1.00	Reference	0.092
≥ 2 chronic conditions	1.34	0.95-1.89	

Multiple regression model (adjusted for age, country and HIV).

Obesity, hypertension, any chronic condition and multimorbidity were the only variables significant at $p < 0.01$ on bivariate analysis and are evaluated in the multivariate analysis.



NB = Non-black

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