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Contribution à la connaissance du fardeau et des facteurs pronostiques du cancer du sein au Bénin et en Afrique au Sud du Sahara

Freddy Gnangnon

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Université
de Limoges

Thèse de doctorat



Université de Limoges cotutelle Université d'Abomey-Calavi
ED 652 - Biologie, Chimie, Santé & EDSS
EpiMaCT- U1094 Inserm UMR270 IRD & LEMACEN

Thèse pour obtenir le grade de
Docteur des Universités de Limoges et d'Abomey-Calavi
Discipline : Santé publique, épidémiologie, environnement et sociétés

Présentée et soutenue par

Freddy Houéhanou Rodrigue GNANGNON

**Contribution à la connaissance du fardeau et des facteurs
pronostiques du cancer du sein au Bénin et en
Afrique au Sud du Sahara**

Le 7 Octobre 2024

Thèse dirigée par :

Pr Pierre-Marie PREUX et Pr Dismand HOUINATO

JURY :

Présidente du jury

Mme. le Professeur Elise DELUCHE, PU-PH, Université de Limoges, France

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Dédicace

Je dédie cette thèse à mon feu père Hospice GNANGNON, à ma mère Julienne GNANGNON née KANHONOU, ainsi qu'à mes sœurs et à mon frère : Judith, Hermine, Chimène, Josiane et José GNANGNON.

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« De toutes les formes d'inégalité, l'injustice en matière de soins de santé est la plus choquante et la plus inhumaine. »

Martin Luther King Homme politique, Religieux américain (1929 - 1968)

SERMENT DU DOCTORANT

« En présence de mes pairs. Parvenu à l'issue de mon doctorat en santé publique, mention épidémiologie, et ayant ainsi pratiqué, dans ma quête du savoir, l'exercice d'une recherche scientifique exigeante, en cultivant la rigueur intellectuelle, la réflexivité éthique et dans le respect des principes de l'intégrité scientifique, je m'engage, pour ce qui dépendra de moi, dans la suite de ma carrière professionnelle quel qu'en soit le secteur ou le domaine d'activité, à maintenir une conduite intègre dans mon rapport au savoir, mes méthodes et mes résultats. »

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Droits d'auteurs

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Liste des abréviations, sigles et acronymes

ADN	: Acide désoxyribonucléique
AIEA	: Agence Internationale de l'Energie Atomique
AJCC	: Joint Committee on Cancer
ASS	: Afrique au Sud du Sahara
ATOM	: Access to Oncology Medicines
BRCA1	: Breast Cancer gene 1
BRCA 2	: Breast Cancer gene 2
CERSS	: Comité d’Ethique de Recherche en Science de la Santé
CHU-MEL	: Centre Hospitalier Universitaire de la Mère et de l’Enfant Lagune
CHD	: Centre Hospitalier Départemental
CIRC	: Centre International de Recherche sur le Cancer
CI5	: Cancer Incidence in Five Continents
CNHU-HKM	: Centre National Hospitalier Universitaire Hubert Koutoukou Maga
COVID 19	: Coronavirus Disease 2019
CRA	: Comptes Rendus d'examen Anatomopathologique
CSTN	: Cancer du Sein Triple Négatif
CTC	: Cellules Tumorales Circulantes
DALY	: Disability-Adjusted Life Years
DDS	: Direction Départementale de la Santé
ECHO	: Extension for Community Healthcare Outcome
FDA	: Formulaire de Demande d'examen Anatomopathologique
GBCI	: Global Breast Cancer Initiative
GLOBOCAN	: Global Cancer Observatory
HER2	: Human Epidermal Growth factor Receptor 2
IARC	: International Agency for Research on Cancer
IHC	: Immunohistochimie
INSTaD	: Institut National de la Statistique et de la Démographie
IRM	: Imagerie par Résonance Magnétique
Ki-67	: Index de prolifération
Micro ARN	: Micro Acide Ribonucléique
MNT	: Maladie Non Transmissible
NCCN	: National Comprehensive Cancer Network
ODD	: Objectif de Développement Durable
OMS	: Organisation Mondiale de la Santé
ONU-SIDA	: Programme commun de l’Organisation des Nations Unies sur le VIH-SIDA
PD-L1	: Programmed death ligand-1
PIB	: Produit Intérieur Brut
RCP	: Réunion de Concertation Pluridisciplinaire
RGPH	: Recensement général de la Population et de l'Habitat
SBR	: Scarff Bloom et Richardson (Grade histopronostique de)
TILs	: Tumor Infiltrating Lymphocytes
THS	: Traitement Hormonal Substitutif
UICC	: Union Internationale Contre le Cancer
VIH-SIDA	: Virus de l'Immunodéficience Humaine- Syndrome d’Immunodéficience Acquise

Introduction

Avec 2,3 millions de nouveaux cas (46,8 % des cancers), le cancer du sein est, depuis 2022, le deuxième cancer le plus diagnostiqué au monde devant le cancer du poumon (Bray et al., 2024). Il est en outre le premier cancer chez la femme dans 159 sur les 185 pays couverts par l'observatoire mondial du cancer (GLOBOCAN) du Centre International de Recherche sur le Cancer (CIRC) de l'Organisation Mondiale de la Santé (OMS) (Bray et al., 2024).

En Afrique au Sud du Sahara (ASS) le cancer du sein est la première cause de morbidité et la deuxième cause de mortalité par cancer (Bray et al., 2022). Bien que les taux d'incidence en ASS soient parmi les plus bas du monde, les taux de mortalité y sont parmi les plus élevés, ce qui reflète des résultats particulièrement médiocres en matière de survie (Joko-Fru et al., 2020).

Plusieurs raisons pourraient expliquer cette mortalité relativement élevée du cancer du sein chez les femmes d'ASS. La première particularité est inhérente aux femmes noires qui sont réputées développer des cancers du sein plus agressifs et par conséquent plus létaux que ceux des femmes issues d'autres origines ethniques. Par exemple, une étude menée aux États-Unis, en 2012, a montré que la mortalité par cancer du sein est 42 % plus élevée chez les Afro-Américaines que chez les Américaines blanches (DeSantis et al., 2016). Pour certains auteurs, le cancer du sein est la plus remarquable des disparités basées sur l'ethnicité en oncologie (Newman & Kaljee, 2017).

En plus de cette susceptibilité, les femmes vivant en ASS sont soumises à des facteurs délétères supplémentaires :

- des considérations socioculturelles spécifiques et péjoratives qui expliquent le diagnostic tardif du cancer du sein et par conséquent une mortalité plus élevée. Une étude réalisée à Cotonou au Bénin a permis de montrer que 65% des cas étaient diagnostiqués à un stade tardif (Tonato Bagnan et al., 2013). Une autre étude réalisée au Nigeria montre que la peur de la mastectomie est la principale cause du diagnostic tardif des cancers du sein (Ajekigbe, 1991).
- l'absence à ce jour de programmes de dépistage organisé dans de nombreux pays d'ASS;
- la faible accessibilité économique et géographique aux moyens de diagnostic et de traitement, particulièrement pour les femmes vivant en zone rurale et dans les déserts médicaux du continent. Même lorsque les modalités diagnostiques et thérapeutiques sont disponibles, elles se heurtent aux préjugés socio-culturels ; ainsi pour une frange de la population d'ASS, le traitement hospitalier entraînerait une aggravation de la maladie, ce qui conduit les patients et les membres de leur famille à refuser ce traitement (Ngwa et al., 2022).

- le faible accès aux soins et le diagnostic tardif sont aggravés par les crises et l’instabilité politique fréquentes sur le continent.

Etonnamment, alors que la plupart des études (Bray et al., 2022; Joko-Fru et al., 2020; Ngwa et al., 2022) ont souligné la nécessité d'une détection précoce pour améliorer la survie, seules quelques études ont examiné les capacités actuelles des hôpitaux à fournir un continuum de soins (Domgue et al., 2023). De plus, les données empiriques et observationnelles relatives à la prise en charge du cancer du sein en Afrique au Sud du Sahara font dramatiquement défaut.

En raison de l’occidentalisation des modes de vie observée en ASS, l’incidence des cancers du sein devrait rapidement augmenter au cours des prochaines décennies (Joko-Fru et al., 2020). Il y a toutefois peu de publications sur les projections à long terme du fardeau du cancer du sein dans les pays d'Afrique subsaharienne. Des études supplémentaires sont donc nécessaires pour comprendre les tendances de l'incidence du cancer du sein dans les pays du continent (Joko-Fru et al., 2020).

Parallèlement à l’incidence, la mortalité du cancer du sein en ASS pourrait substantiellement augmenter du fait notamment des infrastructures et ressources inexistantes ou inadéquates mais également des spécificités culturelles qui constituent parfois une véritable barrière à l’accès aux soins.

Au total, il importe de disposer de données fiables aussi bien sur l’incidence, la mortalité et le pronostic du cancer du sein en ASS que sur la capacité du système de santé à en assurer la prise en charge. Une meilleure compréhension de ces déterminants permettrait de mieux orienter et structurer des politiques ciblées pour la lutte contre ce fléau dans les pays d’ASS tel que le Bénin.

Chapitre I. GENERALITES-PROBLEMATIQUE

I.1. Epidémiologie descriptive et analytique du cancer du sein

I.1.1. Incidence

I.1.1.1. Dans le monde

En 2020, le cancer du sein est devenu le cancer le plus diagnostiqué au monde devant le cancer du poumon (Sung et al., 2022). Ainsi, en 2022, il a été enregistré environ 2,3 millions de nouveaux cas de cancer du sein, soit 11,6 % des cas de cancer dans le monde (Bray et al., 2024). Le cancer du sein est le cancer le plus fréquemment diagnostiqué et la principale cause de décès par cancer chez les femmes (Lei et al., 2021). Il représente 1 cas de cancer chez la femme sur 4, se classant ainsi au premier rang pour l'incidence dans 157 pays sur les 185 couverts par le programme GLOBOCAN du Centre International de Recherche sur le Cancer (CIRC) de l'OMS (Bray et al., 2024) (**Figure 1**).

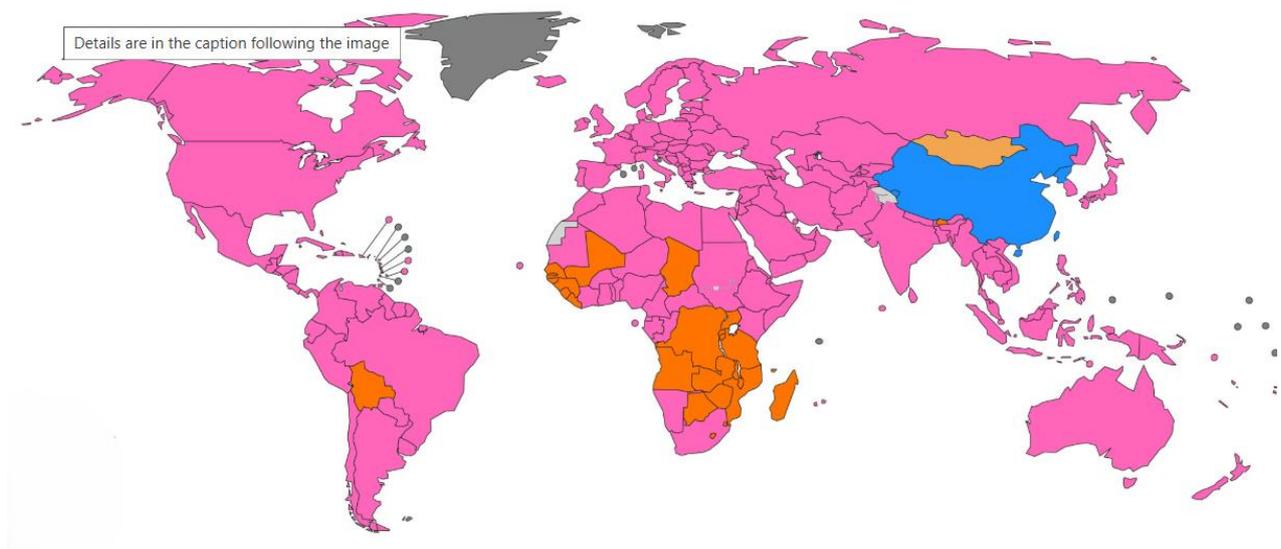


Figure 1 : Répartition des pays en fonction du premier cancer incident chez la femme 2022 (Bray et al., 2024)

Le cancer du sein constitue donc un problème de santé publique majeur, une menace pour la santé des femmes et un obstacle à l'atteinte des objectifs pour le développement durable des Nations Unies. Selon les données de l'OMS, en 2020, les taux d'incidence standardisés par âge pour le cancer du sein parmi les femmes variaient considérablement selon les régions du monde, allant de 27,4 pour 100 000 femmes en Afrique à 92,1 pour 100 000 femmes en Amérique du Nord (Europe : 88,9, Océanie : 68,8, Asie de l'Est : 36,3, Amérique latine et Caraïbes : 32,4) (Bray et al., 2024) (**Figure 2**). La Belgique est le pays rapportant l'incidence la plus élevée au monde (Sung et al., 2022) mais

c'est la Chine qui est le pays qui enregistre le plus grand nombre de cas, représentant environ 18,4 % des cas mondiaux de cancer du sein, suivie des États-Unis avec 11,8 % des cas (Lei et al., 2021).

On remarque également une variation temporelle. Les taux d'incidence du cancer du sein ont uniformément et rapidement augmenté au cours des années 1980 et 1990 dans de nombreux pays développés, reflétant probablement des changements dans la prévalence des facteurs de risque comportementaux, associés à une détection accrue grâce à la généralisation du dépistage. Dans ces même pays, l'incidence a ensuite chuté dans les années 2000 avant de se stabiliser en raison notamment du recul de l'utilisation des traitements hormonaux substitutifs de la ménopause et du plateau de l'adhésion au dépistage. Depuis 2007, on observe une lente remontée des taux d'incidence aux États-Unis, en Europe et en Océanie (Sung et al., 2022).

Parallèlement, les taux d'incidence du cancer du sein augmentent rapidement dans les pays en développement d'Amérique du Sud, d'Afrique et d'Asie où l'incidence était jadis relativement basse. Mais c'est en ASS que l'on observe les augmentations les plus rapides. Cette tendance peut être expliquée par l'occidentalisation galopante des modes de vie observée dans ces régions, provoquée par la croissance économique et l'augmentation de la proportion de femmes dans la main-d'œuvre industrielle (Sung et al., 2022) ; mais également par une amélioration des moyens de diagnostic. A terme, ce processus pourrait aboutir à la réduction des écarts internationaux en matière d'incidence du cancer du sein (Sung et al., 2022).

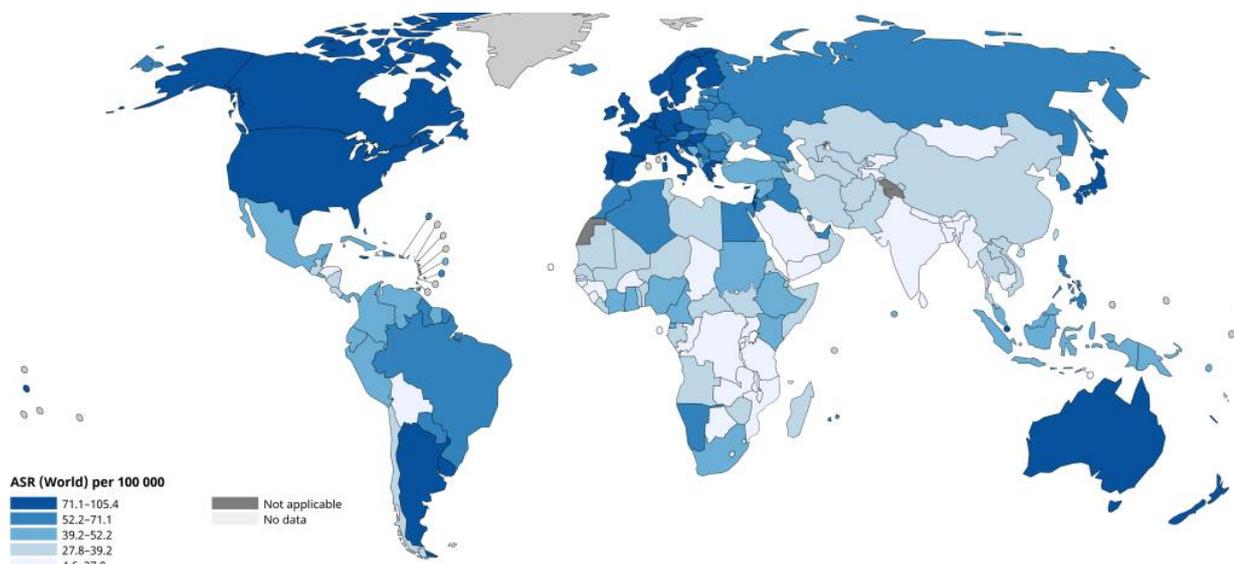


Figure 2 : Taux d'incidence standardisés du cancer du sein dans le monde en 2022 (GLOBOCAN, 2020)

I.1.1.2. En Afrique au Sud du Sahara

Le cancer est un problème majeur de santé publique en ASS, responsable d'un décès prématuré sur sept. Si rien n'est fait, ce fardeau devrait presque doubler au cours des 20 prochaines années, en raison de la croissance démographique et du vieillissement de la population. Pour relever ce défi croissant, chaque pays d'ASS doit mettre en œuvre un programme de lutte contre le cancer. Pour cela, les pays de la région ont besoin de systèmes de surveillance pour mesurer l'ampleur du problème et suivre les progrès de la planification de la lutte contre le cancer.

Afin d'illustrer cette partie, nous avons souhaité insérer un article auquel nous avons contribué (pages suivantes). Le but de ce travail était de présenter les estimations nationales de l'incidence du cancer et de la charge de mortalité dans les pays d'Afrique subsaharienne. Cette étude donne un aperçu des tendances de l'incidence du cancer et de la mortalité par cancer dans les 48 pays d'ASS. Elle situe par ailleurs la place du cancer du sein dans la morbi-mortalité liée au cancer en ASS.

Le nombre de nouveaux cas de cancer et de décès ont été extraits de la base de données GLOBOCAN du Centre International de Recherche sur les Cancers pour l'année 2020. Les estimations nationales ont été élaborées à partir des données enregistrées par les registres du cancer basés sur la population en Afrique au Sud du Sahara tel que le Registre des Cancers de Cotonou (Bénin).

Cette étude a permis d'estimer à 801 392 le nombre de nouveaux cas de cancer en ASS et à 520 158 le nombre de décès par cancer en Afrique au Sud du Sahara en 2020. Avec 129 400 cas chez les femmes, le cancer du sein était le cancer le plus fréquent, occupant la première place en termes d'incidence dans 28 pays d'ASS. Le risque pour une femme d'Afrique de développer un cancer avant l'âge de 75 ans était de 14,1 % et le cancer du sein à lui seul représentait 4,1 % du risque. Avec le cancer col de l'utérus, le cancer du sein représentait plus de la moitié des cancers chez les femmes en 2020, et plus de trois cas sur dix chez les deux sexes. Le cancer du sein était en outre la principale cause de décès par cancer chez les femmes dans 21 pays. Il existait cependant des variations géographiques notables.





Articles

Cancer in sub-Saharan Africa in 2020: a review of current estimates of the national burden, data gaps, and future needs

Freddie Bray PhD ^a  , D Maxwell Parkin MD ^{b, c} on behalf of the African Cancer Registry Network*

Freddy Gnanon, Gontse Tshisimogo, Jean-Felix Peko, Innocent Adoubi, Mathewos Assefa, Lamin Bojang, Baffour Awuah, Moussa Koulibaly, Nathan Buziba, Anne Korir, Charles Dzamalala, Bakarou Kamate, Shyam Manraj, Josefo Ferro, Cesaltina Lorenzoni, Rolf Hansen, Hassan Nouhou, Olufemi Ogunbiyi, Festus Igbinoba, Ima Ekanem, Abidemi Omonisi, Emmanuel Chirpaz, Francois Uwinkindi, Anne Finesse, Ntuthu Somdyala, Elvira Singh, Xolisilie Dlamini, Nestory Masalu, Furaha Serventi, Caroline Mrema, Henry Wabinga, Martin Ogwang, Linda Chiwele, Margaret Borok, Tatenda Chingonzoh

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Available online 9 May 2022.

Cancer in sub-Saharan Africa in 2020: a review of current estimates of the national burden, data gaps, and future needs



Freddie Bray, D Maxwell Parkin, on behalf of the African Cancer Registry Network*

Summary

Background With the cancer burden rising in sub-Saharan Africa, countries in the region need surveillance systems to measure the magnitude of the problem and monitor progress in cancer control planning. Based on the national estimates built from data provided by cancer registries in sub-Saharan Africa, we summarise key patterns of the regional burden and argue for investments in locally produced data.

Methods To present national estimates of the cancer incidence and mortality burden in sub-Saharan Africa countries, new cancer cases and deaths were extracted from International Agency for Research on Cancers' GLOBOCAN database for the year 2020. Given weak vital statistics systems, almost all of the information on the cancer burden in sub-Saharan Africa was derived from population-based cancer registries. Of the 48 countries included in GLOBOCAN (national populations must be larger than 150 000 inhabitants in 2020), relatively recent cancer registry data (up to 2019) were directly used to produce national incidence estimates in 25 countries, while the absence of such data for 16 meant that estimates were based on data from neighbouring countries. Tables and figures present the estimated numbers of new cases and deaths, as well as age-standardised (incidence or mortality) rates per 100 000 person-years and the cumulative risk of developing or dying from cancer before the age of 75 years.

Findings 801 392 new cancer cases and 520 158 cancer deaths were estimated to have occurred in sub-Saharan Africa in 2020. Cancers of the breast (129 400 female cases) and cervix (110 300 cases) were responsible for three in ten of the cancers diagnosed in both sexes. Breast and cervical cancer were the most common cancers, ranking first in 28 and 19 countries, respectively. In men, prostate cancer led in terms of incidence (77 300 cases), followed by liver cancer (24 700 cases) and colorectal cancer (23 400 cases). Prostate cancer was the leading incident cancer in men in 40 sub-Saharan Africa countries. The risk of a woman in sub-Saharan Africa developing cancer by the age of 75 years was 14.1%, with breast cancer (4.1%) and cervical cancer (3.5%) responsible for half of this risk. For men, the corresponding cumulative incidence was lower (12.2%), with prostate cancer responsible for a third of this risk (4.2%). Cervical cancer was the leading form of cancer death among women in 27 countries, followed by breast cancer (21 countries). Prostate cancer led as the most common type of cancer death in 26 countries, with liver cancer ranking second (11 countries).

Interpretation The estimates indicate substantial geographical variations in the major cancers in sub-Saharan Africa. Rational cancer control planning requires capacity to be built for data production, analysis, and interpretation within the countries themselves. Cancer registries provide important information in this respect and should be prioritised for sustainable investment in the region.

Funding None.

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Introduction

Cancer is a major public health problem in sub-Saharan Africa, affecting many of its 1 billion inhabitants. The disease is among the three leading causes of premature death (at ages 30–69 years) in almost all constituent countries,¹ and is responsible for one in seven premature deaths overall and one in four deaths from non-communicable diseases (NCDs).² Currently, the estimated risk of a woman in sub-Saharan Africa dying from cancer before 75 years of age is not dissimilar to that seen in North America and the high-income countries of Europe.³ Even if cancer incidence rates were to remain unchanged, the burden is expected to nearly double in sub-Saharan Africa during the next 20 years as a result of

population growth and ageing, reaching 1.5 million new cases and 1 million deaths by the year 2040 (see the Cancer Tomorrow website).

To overcome this mounting challenge, each country in sub-Saharan Africa needs to implement a cancer control programme as part of national health planning and have at its disposal routine surveillance systems capable of monitoring progress in the delivery of specific interventions.⁴ The need for the collection and evaluation of population-based indicators is well recognised in the context of global cancer surveillance,^{5,6} and the urgency of doing so has been further underscored with the inclusion of targets designed to assess the ongoing scale-up of WHO's three signature

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See Online for appendix

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<https://go.iarc.fr/tomorrow/en>

Research in context**Evidence before this study**

National statistics on cancer burden have been reported regularly by the International Agency for Research on Cancer (IARC) over the past four decades, with the country-level estimates in sub-Saharan Africa derived largely from data provided by population-based cancer registries. Three volumes presenting such recorded data in the region have been published, the most recent including results from 31 population-based cancer registries in 22 sub-Saharan Africa countries. We searched MEDLINE for studies in constituent countries on the cancer burden in sub-Saharan Africa, with search terms including "cancer", "registry", "incidence", "mortality", "Africa", and "estimates" on Dec 15, 2021, without language restrictions, with a focus on publications from 2012 onwards. We retrieved approximately 600 papers and reviewed them for relevant content.

Added value of this study

As well as summarising key patterns of the cancer incidence and mortality burden in sub-Saharan Africa, this study

provides a brief overview of how national estimates of cancer incidence and mortality are built up from data from population-based cancer registries in the region. We discuss the need for investment in such locally produced data.

Implications of all the available evidence

Cancer estimates at the national level are not intended as a surrogate for continuous approaches to data collection from population-based cancer registries and vital registration systems. With the cancer burden expected to nearly double in sub-Saharan Africa in the next 20 years, it is imperative to build capacity and infrastructure for data production, analysis, and interpretation within the countries themselves, as part of cancer control planning, policy formulation, and action.

cancer initiatives on cervical, childhood, and breast cancer.⁷⁻⁹

To determine the scale and distribution of the major cancer types and their continuing evolution at the national and subnational level, three complementary measures are essential—namely, incidence (new cases of disease), survival (percentage of patients surviving a specified number of years after initial diagnosis), and mortality (number of deaths).⁵ Although the availability of high-quality mortality data has been shown to be associated with improved population health outcomes¹⁰ and is considered to be the ultimate indicator of progress,¹¹ most sub-Saharan African countries have weak civil registration and vital statistics systems. There are no continuous or permanent sources of cause-specific mortality data other than in Mauritius, Seychelles, and South Africa.¹² Indeed, only about 6% of the region is currently covered by reasonably accurate (considered to be of medium or high quality) death registration systems.¹³

As a result, almost all of our information on the cancer burden in sub-Saharan Africa is derived from population-based cancer registries. Population-based cancer registries are providers of statistics on cancer incidence and survival (the two metrics from which mortality can be calculated). They are, therefore, a crucial resource for policy makers, providing the evidence base from which to plan, monitor, and assess the effectiveness of national cancer control programmes.

Cancer registration in sub-Saharan Africa has been slow to develop,^{14,15} with few centres able to report their results in the reference publication *Cancer incidence in five continents* (CI5), which compiles comparable cancer incidence rates across registry populations worldwide.¹⁶ However, in the past decade, the Global Initiative for

Cancer Registry Development (GICR) led by the International Agency for Research on Cancer (IARC) has given new impetus to the support of existing cancer registries and in aiding the establishment of new ones. In sub-Saharan Africa, the work of the GICR is done by members of the African Cancer Registry Network (AFCRN; appendix p 1). AFCRN is a consortium of all population-based cancer registries in sub-Saharan Africa that can meet defined criteria of quality, including progressively complete population coverage. The number of such registries in sub-Saharan Africa had increased from 21 in 2013 to 35 (in 25 different countries; figure 1) by the end of 2021.¹⁷

We briefly report the cancer burden in terms of numbers and patterns of cancer across the region using IARC's GLOBOCAN 2020 national cancer incidence and mortality estimates (see the Cancer Today website),^{3,18} built up using the recorded data provided by population-based cancer registries in sub-Saharan Africa. We argue for an investment in such registries in the region to attain better region-wide estimates and, more importantly, to provide individual countries with the necessary data to plan and inform cancer services.

Methods**Data sources and estimation of incidence**

The number of new cancer cases and deaths were extracted from the GLOBOCAN database, which presents estimates of the incidence of, and mortality from, all cancers and 36 major cancer types in 185 countries or territories worldwide by sex and 18 age groups in 5-year bands (from 0–4 years to ≥85 years) for the year 2020.^{3,18} Corresponding population data for the same year were extracted from the UN website.¹⁹ The

For more on the African Cancer Registry Network see <http://afrco.org>

For the GLOBOCAN database see <https://gco.iarc.fr/today/home>

For Cancer Today see <https://gco.iarc.fr/today/home>

For more on the Global Initiative for Cancer Registry Development see <http://gicr.iarc.fr>

data sources and hierarchy of methods used in compiling the cancer estimates have been described in detail elsewhere.¹⁸ Their assembly relies on the best available data on cancer incidence and mortality at the country level. The sources and methods of each iteration of the GLOBOCAN estimates have been documented in detail^{18,20,21} and are available online by country,²² and the methods for deriving national incidence estimates have been validated.²³ Uncertainty intervals (UIs), developed to provide an error range for the site-specific and sex-specific numbers of cancer cases and deaths, are available on the Cancer Today website. UIs are based on the SE of the rates used in the estimation corrected for three major sources of bias: coverage of the national population, the lag time (recency of recorded data relative to year of estimation), and the data quality (completeness and validity of recorded data);²⁰ the methods of estimation and penalties used are also available online by country.²⁴

For the sub-Saharan African region, the main source of recorded data is the updated cancer registry incidence data made available via the AFCRN.¹⁷ The sources of local data and methods used to estimate incidence in each country are summarised in the appendix (p 2). Of the 48 countries in sub-Saharan Africa included in GLOBOCAN (national populations had to have >150 000 inhabitants in 2020), relatively recent cancer registry data were used for 25, and the absence of any recent data for 16 nations meant that estimates were based on data from neighbouring countries.

Figure 2 depicts the data sources available in each country and the methods used to make national estimates for 2020. Cancer registries covering the entire (national) population are present in Botswana, Eswatini, the Gambia, La Réunion, Mauritius, Namibia, Rwanda, and South Africa. Although none of these registries were of a quality sufficient for inclusion in the latest volume (XI) of CI5,¹⁶ the incidence rates from those of Botswana, Eswatini, the Gambia, La Réunion, Mauritius, Namibia, and Rwanda were used directly to generate estimates for the country. Several subnational registries covering less than 10% of the national population were, however, included in CI5 (Kenya [Nairobi], Seychelles, South Africa [Eastern Cape], Uganda [Kyadondo], and Zimbabwe [Harare, African population]). A further 14 countries had local (ie, subnational) registries that cover less than 10% of the national population; although none appeared in CI5, the incidence data were compiled in the monograph *Cancer in Sub-Saharan Africa Volume III*,²⁵ and those data were used to estimate national incidence. 17 countries had no sources of incidence information (figure 2).

Data sources and estimation of mortality

Cancer-specific mortality statistics were available from five countries (Cape Verde, La Réunion, Mauritius, São Tomé and Príncipe, and South Africa; data not shown). For La Réunion, Mauritius, and South Africa, the trends in rates from up to 2018 were projected to

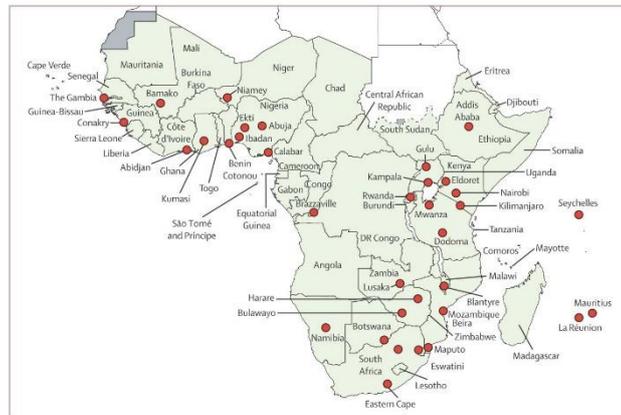


Figure 1: Members of the African Cancer Registry Network as of Jan 1, 2022

and applied to the 2020 population. Data from up to 2012 of modest quality were used for the 2020 estimates of Cape Verde and São Tomé and Príncipe. For the remaining 43 countries, mortality was estimated from incidence using mortality-to-incidence ratios from the Black population of the USA, scaled by the ratio of the Human Development Index (HDI) of the US population and that of the country concerned.¹⁸ For breast, cervical, and childhood (at ages 0–14 years) cancers, mortality was estimated from incidence estimates and modelled survival, as described previously.²¹

Statistical analysis

We present estimated numbers of new cases and deaths, alongside 95% UIs (appendix p 3). We also use two summary measures based on direct standardisation—namely, the age-standardised incidence or mortality rate per 100 000 person-years based on the world standard population proposed by Segi and Kurihara²⁶ and modified by Doll and colleagues,²⁷ and the cumulative risk of developing or dying from cancer in a lifetime, expressed as a percentage, assuming the absence of competing causes of death.²⁸ These measures allow comparisons between populations adjusted for differences in age structures. The age-standardised rate is presented for all ages combined, and the cumulative risk is presented for ages 0–74 years, given competing risks of death from other causes intensify at older ages (≥ 75 years).²⁸ All analyses were done in Stata (version 14.0).

The Global Cancer Observatory includes facilities for the tabulation and graphical visualisation of the GLOBOCAN database, including explorations of the current and future burden for 36 cancer types, and all cancers combined, including non-melanoma skin cancer (International Classification of Diseases-10 C44 excluding basal-cell carcinomas).

For the Global Cancer Observatory see <https://gco.iarc.fr>

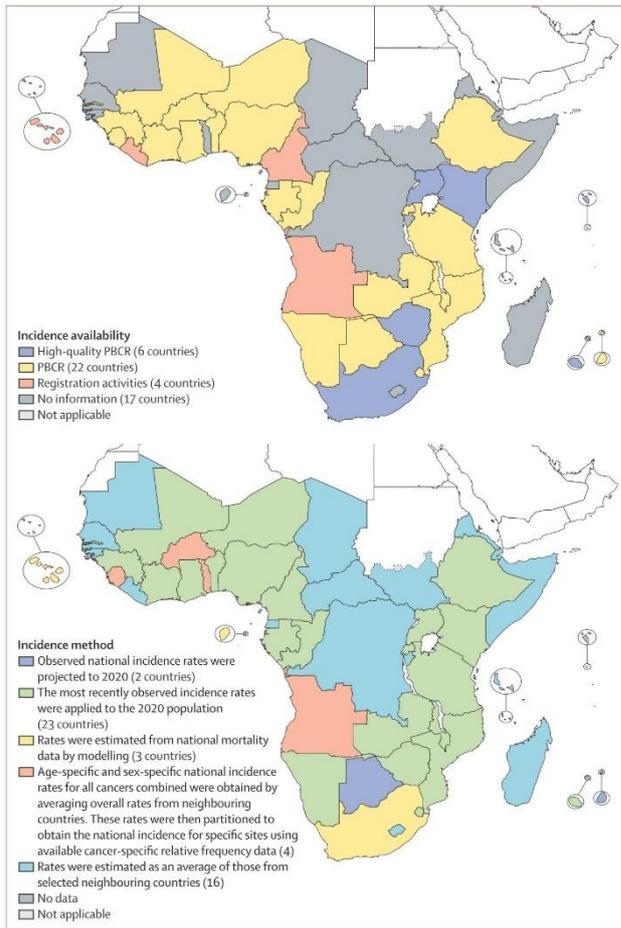


Figure 2: The sources of incidence data available in sub-Saharan Africa and the methods used to produce the GLOBOCAN national estimates in 2020

Seychelles is included as a member of the African Network of Cancer Registries on the top map, but excluded from the bottom map, as GLOBOCAN estimates are not made for populations of 150 000 or fewer inhabitants. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there might not yet be full agreement. PBCR=population-based cancer registry.

Role of the funding source

There was no funding source for this study.

Results

Overall, 801 392 new cancer cases (4.2% of the world total of 19.3 million cases) and 520 158 cancer deaths (5.2% of the world total 9.9 million cases) were estimated

to have occurred in sub-Saharan Africa in 2020 (table). Cancers of the breast (129 400 [27.3%] of 474 000 female cases) and cervix (110 300 [23.3%] female cases) were responsible for three in ten of the cancers diagnosed in both sexes combined in 2020 (figure 3). In men, the highest number of new diagnoses was for prostate cancer (77 300 [23.6%] of 327 000 male cases), followed by liver cancer (24 700 [7.6%] male cases) and colorectal cancer (23 400 [7.2%] male cases).

The risk of a woman in sub-Saharan Africa developing cancer by the age of 75 years was almost 14.1%, with breast cancer (4.1%) and cervical cancer (3.5%) responsible for half of this risk (figure 4). For men, the corresponding cumulative incidence of cancer was lower (12.2%), with prostate cancer responsible for a third of this risk (4.2%; figure 4). Across the sub-Saharan Africa region, substantial geographical variations were seen in these, and other, important cancers by sex (appendix p 4). Figure 5 shows the most numerous cancers in each country by sex; in men, the leading incident cancer in was prostate cancer (in 40 sub-Saharan Africa countries), whereas in women, the most common cancers were breast cancer (in 28 countries) and cervical cancer (in 19 countries).

In GLOBOCAN 2020, ratios of mortality to incidence, rather than survival, were used to estimate mortality for most cancer types; for this reason, geographical patterns of mortality tend to follow closely those of incidence (table). Figure 4 shows the cumulative mortality for the ten major cancers in sub-Saharan Africa, and shows that cervical cancer was the leading form of mortality in women, with a 2.6% risk of dying from this cancer by the age of 75 years. It was the leading cause of death from cancer among women in 27 countries, more than for breast cancer (21 countries; figure 5). As with incidence, prostate cancer was the most common cause of death from cancer in men, albeit in fewer countries than for incidence (26), with liver cancer ranking in first position in 11 countries.

Discussion

This study provides a brief overview of the patterns of cancer incidence and mortality across the 48 countries of sub-Saharan Africa, using IARC's current national estimates for the year 2020. Cancers of the female breast and cervix dominate the regional cancer landscape. In combination, these two cancers were responsible for more than half the cancer cases in women in 2020, and three in ten cases in both sexes. They trade off as the leading causes of cancer incidence and mortality in women across the countries in the region. Prostate cancer was responsible for almost a quarter of all cases in men, and, as noted previously,²⁹ the risk of developing the disease before the age of 75 years of 4.2%, affecting almost one in 25 men, is quite similar to the equivalent risks for breast (4.1%) and cervical cancer (3.5%) among women in sub-Saharan Africa. There are, however, notable geographical variations by sex, and in men, liver cancer and Kaposi sarcoma are the leading causes of

	Population size (millions)	HDI	Incidence in men		Incidence in women		Incidence in both sexes		Mortality in men		Mortality in women		Mortality in both sexes				
			Cases	Age-standardised rate per 100,000 person-years*	Cases	Age-standardised rate per 100,000 person-years*	Cases	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Mortality-to-incidence ratio
Total	1093.99	..	327213	..	474179	..	801392	..	219.991	..	300.267	..	520.158	..	1093.99
Percentage of world total	14.0%	..	3.3%	..	5.1%	..	4.2%	..	4.0%	..	6.8%	..	5.2%	..	14.0%
Eastern Africa																	
Burundi	11.89	Low	3288	129.8	4641	143.6	7929	135.5	2413	100.3	3288	109.0	5701	103.8	0.72	0.67	0.67
Comoros	0.87	Low	228	97.7	381	128.4	609	111.8	161	70.2	250	89.2	411	79.0	0.67	0.67	0.67
Djibouti	0.99	Low	286	71.5	479	112.9	765	91.0	213	55.2	314	76.9	527	65.3	0.69	0.69	0.69
Eritrea	3.55	Low	882	79.0	1526	122.0	2408	100.8	639	59.4	1031	84.5	1670	72.1	0.69	0.69	0.69
Ethiopia	114.96	Low	26754	77.9	50598	134.2	77352	106.7	18895	58.0	32970	91.7	51865	75.4	0.67	0.67	0.67
Kenya	53.77	Medium	15566	133.2	26550	168.2	42116	149.2	10466	96.5	16626	112.6	27092	103.2	0.64	0.64	0.64
La Réunion	0.90	Very high	1713	256.9	1252	173.9	2965	212.5	919	130.2	604	71.0	1523	97.8	0.51	0.51	0.51
Madagascar	27.69	Low	8234	111.4	12447	137.9	20681	124.3	5811	82.3	8026	93.9	13837	87.8	0.67	0.67	0.67
Malawi	19.13	Low	6723	133.3	11213	177.8	17936	154.2	4679	98.4	7775	130.3	12454	113.4	0.69	0.69	0.69
Mauritius	1.27	High	1364	150.0	1686	166.3	3050	155.0	742	79.7	762	68.2	1504	72.4	0.49	0.49	0.49
Mozambique	31.26	Low	10040	128.7	15406	144.0	25446	135.3	7048	95.4	10966	106.9	18014	100.4	0.71	0.71	0.71
Rwanda	12.95	Low	3683	112.8	5152	119.0	8835	113.9	2584	82.7	3460	83.2	6044	81.4	0.68	0.68	0.68
Somalia	15.89	NA†	3723	90.8	6411	144.5	10134	118.2	2827	72.4	4612	108.9	7439	90.9	0.73	0.73	0.73
South Sudan	11.19	Low	2686	87.9	3626	102.5	6312	94.7	2016	68.1	2617	77.0	4633	73.2	0.73	0.73	0.73
Tanzania	59.73	Low	15299	119.7	25165	151.1	40464	133.7	10798	88.5	16147	102.9	26945	94.3	0.67	0.67	0.67
Uganda	45.74	Low	14529	156.4	19479	158.1	34008	153.8	10014	115.5	12978	114.5	22992	112.4	0.68	0.68	0.68
Zambia	18.38	Medium	5968	166.6	7863	154.4	13831	153.5	3791	113.2	4881	103.4	8672	103.3	0.63	0.63	0.63
Zimbabwe	14.86	Medium	5744	198.5	10339	213.9	16083	200.4	3946	142.8	6730	145.3	10676	139.4	0.66	0.66	0.66
Middle Africa																	
Angola	32.87	Medium	8774	135.1	11553	130.5	20327	130.6	5685	92.5	6914	84.1	12599	86.5	0.62	0.62	0.62
Cameroon	26.55	Medium	8510	120.7	12235	138.0	20745	127.7	5648	84.9	7551	90.9	13199	86.6	0.64	0.64	0.64
Central African Republic	4.83	Low	1063	94.8	1612	109.4	2675	100.4	799	74.5	1158	81.8	1957	76.8	0.73	0.73	0.73
Chad	16.43	Low	3433	90.5	5142	114.8	8575	102.3	2538	70.6	3545	84.6	6083	77.3	0.71	0.71	0.71
Democratic Republic of the Congo	89.56	Low	21647	103.0	27222	105.7	48839	102.9	15571	76.0	18841	76.0	34412	74.9	0.70	0.70	0.70
Equatorial Guinea																	
Equatorial Guinea	1.40	Medium	417	101.8	510	126.5	927	110.1	288	73.8	304	82.5	592	76.2	0.64	0.64	0.64
Gabon	2.23	High	718	101.6	1032	132.5	1750	115.8	468	67.9	562	75.9	1030	71.5	0.59	0.59	0.59
Republic of the Congo	5.52	Medium	1105	92.8	1373	81.7	2478	84.4	762	65.6	833	51.9	1595	56.6	0.64	0.64	0.64
São Tomé and Príncipe	0.22	Medium	81	159.1	70	103.0	151	126.4	55	106.2	48	70.0	103	84.5	0.68	0.68	0.68

(Table continues on next page)

	Population size (millions)	HDI	Incidence in men			Incidence in women			Incidence in both sexes			Mortality in men			Mortality in women			Mortality in both sexes		
			Cases	Age-standardised rate per 100,000 person-years*	Cases	Age-standardised rate per 100,000 person-years*	Cases	Age-standardised rate per 100,000 person-years*	Cases	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*	Deaths	Age-standardised rate per 100,000 person-years*
(Continued from previous page)																				
Southern Africa																				
Botswana	2.35	High	839	114.1	1171	109.9	2010	109.5	494	70.9	618	60.3	1112	63.4	0.55					
Eswatini	1.16	Medium	349	112.5	643	156.4	992	127.9	224	77.4	389	97.7	613	82.2	0.62					
Lesotho	2.14	Low	670	99.4	1206	125.3	1876	109.0	460	71.3	796	83.2	1256	74.8	0.67					
Namibia	2.54	Medium	1441	222.0	1904	191.9	3345	198.3	829	133.2	1047	109.6	1876	116.1	0.56					
South Africa	59.31	High	51059	242.1	57109	194.2	108168	209.6	27571	132.7	29231	100.3	56802	111.7	0.53					
Western Africa																				
Benin	12.12	Low	3130	104.7	3617	92.8	6747	95.9	2265	79.6	2397	64.0	4662	69.3	0.69					
Burkina Faso	20.90	Low	4305	96.1	7740	128.1	12045	112.0	3248	74.7	5447	94.1	8695	84.4	0.72					
Cape Verde	0.56	Medium	405	221.7	420	157.9	825	179.0	262	146.1	226	84.0	488	107.6	0.59					
Côte D'Ivoire	26.38	Low	7404	108.6	9896	139.5	17300	133.3	5220	79.6	6540	97.9	11760	88.1	0.68					
Ghana	31.07	Medium	9931	103.7	14078	129.0	24009	115.9	7172	77.9	8630	84.0	15802	80.6	0.66					
Guinea	13.13	Low	2802	110.8	5069	122.5	7871	116.6	2190	89.3	3698	92.6	5888	90.7	0.75					
Guinea-Bissau	1.97	Low	407	97.8	720	118.7	1127	107.2	318	78.5	518	89.5	856	83.3	0.74					
Liberia	5.06	Low	1431	109.8	2121	130.8	3552	119.3	1096	86.0	1507	96.5	2603	90.5	0.73					
Mali	20.25	Low	5198	116.9	8987	162.9	14185	140.3	3927	93.6	6307	120.8	10234	107.5	0.72					
Mauritania	4.65	Low	1209	98.1	1870	121.6	3079	108.6	884	74.7	1237	84.0	2121	78.3	0.69					
Niger	24.21	Low	4107	66.9	5680	89.7	9787	78.4	3339	56.9	4043	67.5	7382	62.2	0.75					
Nigeria	206.14	Low	51388	98.8	73417	122.5	124815	110.4	34200	70.7	44699	79.5	78899	74.8	0.63					
Senegal	16.74	Low	4085	105.2	7232	132.4	11317	119.5	3024	81.0	4869	93.5	7893	87.4	0.70					
Sierra Leone	7.98	Low	1836	92.4	2872	114.6	4708	102.1	1389	73.0	2000	83.2	3389	76.9	0.72					
The Gambia	2.42	Low	460	74.9	575	83.7	1035	79.5	395	65.8	415	65.7	810	65.7	0.78					
Togo	8.28	Low	2319	114.2	2889	111.8	5208	111.8	1608	83.9	1860	76.3	3468	79.1	0.67					

HDI=Human Development Index. NA=not available. *Based on world standard population.^{30,31} For Somalia, there is very little data on the level of national economic development in the country due to political instability and the ongoing conflict.

Table: Sex-specific cases, deaths, age-standardised rates (world), and mortality-to-incidence ratios for all cancers combined, by country and region in sub-Saharan Africa

cancer death in several countries in western and eastern Africa, respectively. These variations probably reflect a varying prevalence and distribution of exposures and, possibly, susceptibility of the underlying populations to them.

It is important for users of the GLOBOCAN database in individual countries to realise how the estimates have been prepared and that, for the most part, they are based on locally produced data, rather than complex modelling that is neither transparent nor reproducible, often based on the prevalence of covariates. We argue, in line with others,^{30,31} that it is important to build capacity and infrastructure for data production, analysis, and interpretation within the countries themselves to inform local planning. The knowledge that their estimates are derived from surveillance systems (cancer registries, or, rarely, civil registration and vital statistics systems) is a powerful incentive to invest in capacity to record routine cancer data in local settings. Yet the importance of local cancer surveillance systems goes way beyond the ability to contribute to global databases. They provide important information (eg, local variations in incidence by residence, ethnicity, stage of disease at diagnosis, and survival by age) for the planning of cancer control interventions and monitoring outcomes of cancer control interventions.^{32,33} None of this information can be obtained through statistical models.

The GICR was established in 2012 as a means of improving the quantity and quality of cancer registry data worldwide, with specific emphasis on low-income and middle-income countries. The AFCRN, founded in 2012, has partnered with IARC to provide a network Regional Hub for cancer registration in sub-Saharan Africa. The AFCRN aims to improve the effectiveness of cancer surveillance by providing expert evaluations of population-based registries and the technical assistance to resolve identified issues. The importance of attaining quality-assured local data in harnessing political will and clinical commitment has been documented.³² The Regional Hub region includes 46 English, French-speaking, and Portuguese-speaking countries, and membership of the AFCRN is available only after an evaluation of the data quality of population-based registration. Specifically, the registries must be evaluated as recording 70% or more of the cancer cases in the populations that they serve. The reason is that their results must be usable for making confident predictions of the cancer patterns and trends, for the purposes of planning and evaluation. In addition, of course, a criterion related to quality is an incentive to improve newly founded or existing registries.

As of Jan 1, 2022, the AFCRN had 35 members in 25 countries. A major weakness in this study is that more than 20 countries in the region still have no adequate cancer surveillance capacity. The reasons for the relative under-development of cancer registration in sub-Saharan Africa have been described many times:¹⁴ insufficient

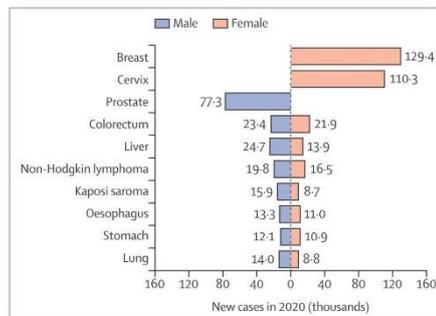


Figure 3: Estimated numbers of cases of the ten most frequent cancers, by sex, in sub-Saharan Africa

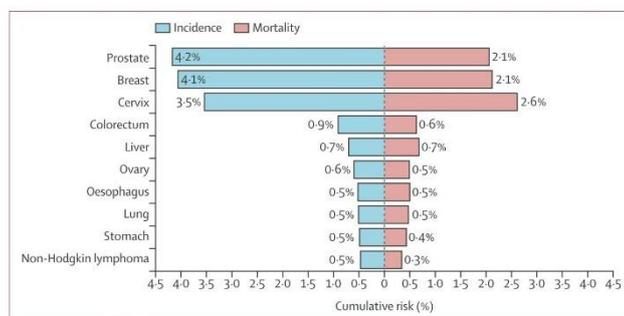


Figure 4: Cumulative risk (at ages 0-74 years) of the ten most frequent cancers in terms of incidence or mortality in sub-Saharan Africa

coordination of data sources, a scarcity of adequate trained technical staff, absence of up-to-date population census figures, poor health infrastructure, insufficient political will, and poor procurement systems marred by mismanagement and corruption.

Computer-based medical information systems remain underdeveloped in sub-Saharan Africa, which means that identification of new cases and the follow-up of patients with cancer are tiresome and expensive. Although the situation is improving, it remains unsatisfactory—all countries should aspire to a national cancer control plan—which in turn requires an adequate cancer information system. The availability of modelled estimates of morbidity and mortality seems reassuring—policy makers get a false impression of certainty about health status and trends, which detracts from making much needed investments to improve data collection and analytical capacity within countries. The problem is, of course, that in most sub-Saharan Africa countries, there is no or insufficient governmental budget for cancer registries. Indeed, many cancer plans do not have a dedicated budget either,^{3,34} and, because cancer registries

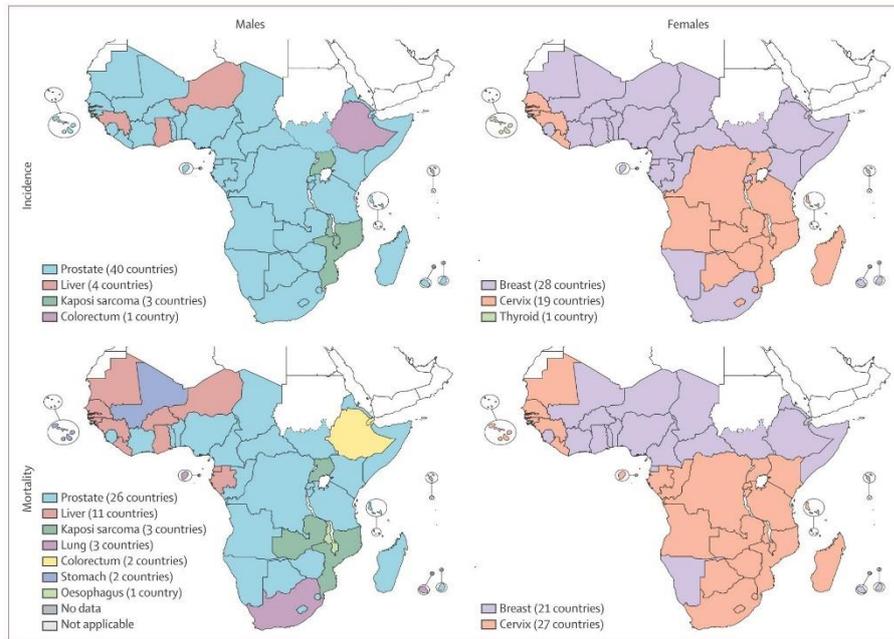


Figure 5: Leading cancers in each country in terms of incidence and mortality, by sex
 The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there might not yet be full agreement.

do not show any immediate effect on cancer prevention or care, their need is not always recognised and appreciated. Historically, registries in Africa have been supported by a wide range of funding agencies, which do not always include health ministries or local health departments. In fact, population-based registries are not costly to establish or maintain.³⁵ A 2019 study estimated the cost of cancer registration at the population level as 1–2 US cents per person in the three lower-income or lower-middle-income countries studied (Kenya, Uganda, and Zimbabwe).³⁶

International partners such as IARC and AFCRN, alongside other supporters working to improve health information systems, such as the Data for Health initiative, funded by Bloomberg Philanthropies,³⁷ can provide technical support and training, and sponsor shorter-term projects. However, sustainability requires local investment, which is often problematic, given the multiple calls on health budgets and limited administrative infrastructures. This said, international researchers tend to consider cancer registry data from low-income countries as a free resource. Some consideration of the local costs in obtaining and treating cancer data in low-income settings

should be part of any budget for research projects that will draw upon such databases.

The GLOBOCAN 2020 database can be considered the most accurate set of estimates presently available given existing data sources. As well as the need for investment in population-based cancer registries, the scarcity of mortality data in sub-Saharan Africa remains a major concern. In the absence of actual data on mortality from cancer, numbers (and rates) of deaths can be estimated from incidence and survival (from population-based cancer registries). However, the current GLOBOCAN estimates for sub-Saharan Africa rely on the observed association between survival and HDI,²⁰ with mortality-to-incidence ratios appropriate to HDI level used as a proxy for survival.^{38,39} With the results of the SurvCan-3 project, benchmarking recent survival probabilities in more than 30 low-income and middle-income countries (unpublished), the mortality estimates in sub-Saharan Africa in future iterations should be more robust than those in the current one.

Many sub-Saharan Africa countries are facing a double burden of increasing NCDs and a residual burden of infectious diseases. Cancer is among the top three causes

of premature death in the vast majority of countries in the region according to WHO estimates for 2019,¹ and NCDs are predicted to surpass communicable, maternal, neonatal, and nutritional diseases as the leading cause of mortality in the region by 2030.⁴⁰ The GLOBOCAN 2020 estimates presented here signal that within the prism of cancer, several cancers with infectious origins (eg, cervical, liver, and Kaposi sarcoma) are still highly prevalent,^{41,42} and neoplasms associated with ill-defined westernisation factors (such as dietary change, obesity, and lack of exercise), which include female breast, prostate, and colorectal cancer, are on the ascent. Cervical cancer incidence rates in southern, eastern, and western Africa, are, as an example, the highest in the world, and there is evidence from recent data from the constituent AFCRN member registries that incidence rates are uniformly rising,⁴³ with one of the determinants—the high prevalence of HIV infection.⁴⁴ Female breast cancer incidence is also rising in many sub-Saharan Africa registries, with the rate of increase varying by population and a generational increase seen in successive cohorts of women aged 45 years or older in Uganda and Zimbabwe.^{45,46} There are also notable variations in breast cancer survival observed across sub-Saharan Africa populations, with lower survival seen among patients diagnosed at a later stage and in countries with a low HDI.⁴⁶ The risk of prostate cancer—already the most common cancer in men in sub-Saharan Africa—is also on the increase in many countries, in part due to increased diagnostic capacity.⁴⁷

A coordinated approach to implementing national strategies, including scale-up of the recent WHO signature initiatives on cervical and breast cancer, must include a sustainable investment in the best-buy surveillance system that provides data on incidence and survival by cancer type and stage at diagnosis. After all, only population-based cancer registries can provide concrete answers to policy makers' enquiries as to whether genuine (population-level) progress is being made in reaching prescribed national targets, such as a cervical incidence rate of 4 or lower per 100 000 women,⁹ or the detection of at least 60% of breast cancers at stages I or II.⁷ Local data from cancer registries are pivotal in improving outcomes and saving lives. It is time to invest in the real world and not a mathematical representation of it.

Contributors

FB and DMP conceptualised and designed the study, and have accessed and verified the data. AFCRN collaborators collected and provided the data. FB and DMP analysed and interpreted the data. FB and DMP drafted and edited the manuscript. Both authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

GLOBOCAN estimates are available at IARC's Global Cancer Observatory. Cancer registry data are available via application to the AFCRN Research Committee.

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For IARC's Global Cancer Observatory see <http://gco.iarc.fr>
For application to the AFCRN Research Committee see <https://afcrn.org/index.php/research/how-to-apply>

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I.1.1.3. Au Bénin

L'absence de statistiques complètes sur la mortalité dans presque tous les pays africains implique que les données sur l'incidence du cancer et la survie provenant des registres du cancer basé sur la population sont essentielles pour la surveillance et le suivi du cancer. Au Bénin, pays d'Afrique de l'Ouest, il n'existe actuellement aucun programme organisé de dépistage du cancer du sein.

Le Ministère de la Santé a mis en place en 2014 un registre du cancer basé sur la population pour la capitale économique du pays. Les données d'incidence du registre des cancers de population de Cotonou (Bénin) pour la période triennale 2014-2016 sont présentées dans l'article suivant auquel j'ai contribué. Il s'agit des premières données sur l'incidence du cancer au Bénin, qui seront précieuses pour l'élaboration et l'évaluation du plan national de lutte contre le cancer. Le but de ce travail était de présenter les estimations de l'incidence du cancer dans la ville de Cotonou au Sud du Bénin. Cette étude permet par ailleurs de déterminer l'incidence du cancer du sein et de situer la place de ce cancer dans la morbidité liée au cancer à Cotonou.

La population moyenne de la ville de Cotonou pour la période 2014-2016 était estimée à 719 712 habitants (378 745 femmes et 340 967 hommes), soit 6,8 % de la population totale du Bénin pour la même période. Au total, 1 086 cas de cancer ont été enregistrés, 608 cas (56,0%) chez les femmes (correspondant à un taux d'incidence annuelle standardisé sur l'âge de 78,4 pour 100 000) et 478 cas (44,0%) chez les hommes (91,8 pour 100 000). Chez les femmes, le cancer du sein était le cancer le plus fréquent, représentant 32,1 % de tous les cas, avec un taux d'incidence annuelle standardisé sur l'âge de 22,6 pour 100 000. Le cancer du col de l'utérus arrive en deuxième position (17,1 %), avec un taux d'incidence annuelle standardisé sur l'âge de 14,9 pour 100 000). Ces deux cancers représentaient près de la moitié de tous les cancers féminins. Sur une échelle semi-logarithmique, les taux d'incidence du cancer du sein par âge montrent que chez les femmes, le cancer du sein commence à un jeune âge (20-24 ans) avec une augmentation régulière et relativement peu de changement dans l'incidence après un pic entre 50 et 54 ans.



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Cancer incidence in Cotonou (Benin), 2014–2016 First results from the cancer Registry of Cotonou

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ABSTRACT

Incidence data from the population cancer registry of Cotonou (Benin) for the three year period 2014–2016 are presented.

1086 cancer cases were recorded, 608 cases (56.0%) in women (corresponding to an age standardized incidence rate (ASR) of 78.4 per 100,000) and 478 cases (44.0%) in men (ASR 91.8 per 100,000).

Breast and cervical cancer accounted for 49.2% of all cancers in women. Breast cancer (ASR 22.6 per 100,000) was more common than cervical cancer (ASR 14.9 per 100,000) and the mean age of cases was lower. The incidence of prostate cancer (one quarter of all cancers in men), 30.5 per 100,000, was similar to that in other West African registries. Cancers of the liver and digestive tract were also relatively common in both sexes.

These are the first data on cancer incidence in Benin, and will be invaluable for the development and evaluation of the National Cancer Control plan.

1. Introduction

Cancer has become a major global public health issue in developed and developing countries and is now one of the leading causes of death in both. In 2018, 9.6 million deaths were attributable to cancer, representing about one in six of all deaths worldwide. With 18.1 million new cases each year, in 2018 more than 43.8 million people were living with cancer [1].

In Africa, the number of new cases was estimated as 1.06 million in 2018 (5.8% of the world total) while the number of deaths was 693,000 (7.3% of the world total). The number on new cases is projected to increase by at least 46% between 2018 and 2030 [1].

The absence of comprehensive mortality statistics for almost all African countries means that data on cancer incidence and survival from population-based cancer registries are essential for cancer surveillance and monitoring, as components of national cancer control plans [2,3]. In Benin, the Ministry of Health established a population-based cancer registry for the capital city of Benin in 2014, under the control of the National Programme for Control of non-Communicable Diseases (PNLMNT). Cancer services in Benin are provided almost entirely through tertiary level hospitals, and in the absence of universal

health coverage, most treatment costs are met by out-of-pocket expenditure. Currently there are no population-based, organized cervical and breast cancer screening programmes in the country

The current report presents the results of the first 3 years of registration (2014–2016) and compares these with the results of other registries in the region, and with the black population of the United States.

2. Material and methods

2.1. Population coverage

The population covered by the registry is comprised of all individuals normally resident in the city of Cotonou, the capital of the Republic of Benin. The size of this population, by 5-year age group and sex, for the years 2014–2016, was estimated based on the most recent population and the housing census (for the year 2013) [4]. The mean average population for the period 2014–2016 was 719,712 (378,745 women and 340,967 men) or 6.8% of the total population of Benin (Fig. 1).

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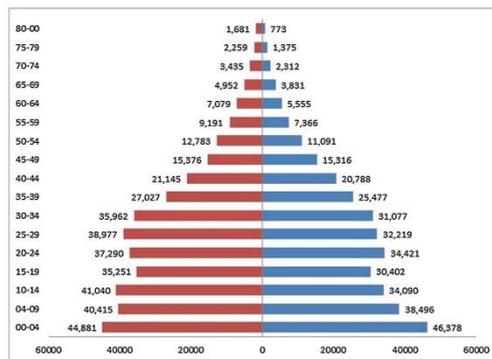


Fig. 1. Population data for the city of Cotonou in 2013 [4].

2.2. Collection and management of data

The registry uses the methods and definitions of the Standard Operating Procedure Manual of the African Cancer Registry Network [5]. Malignant cancers at all sites are registered, regardless of the basis of diagnosis (based on pathology, imaging, tumour markers, or clinical examination alone). Data collection is active, through regular visits to some 28 sources where cancer patients who are residents in the registry's target area are likely to have been diagnosed and / or treated:

- 9 public Health Facilities
- 14 private clinics
- 5 pathology laboratories

The National University Hospital of Cotonou (CNHU-HKM) is the most important source of information for the registry. Appropriate data collection methods have been put in place according to each source of information. In the period studied, there were no specialist oncology services; the Cotonou Private Centre of Oncology became operational only in 2018.

Information on the cancer case (personal data of the patient, details of the tumour and its treatment, the source of information, and the outcome for the patient (alive or dead)) are abstracted from the records in the data sources onto data collection forms. Several items of information are coded (using the International Classification of Diseases for Oncology (ICD-O 3) [6] for the site and morphology of the tumour), before entry of all the information into a database managed by the CanReg5 software developed by the International Agency for Research on Cancer (IARC) [7].

2.3. Quality and completeness of the data

Data capture, quality control and data consistency are performed by the software DepEdits and IarcTools that are integrated into the CanReg5 system [8].

In order to ensure the completeness of ascertainment of cancer cases among Cotonou residents, one or two visits per year are made to health facilities outside of the catchment area which have facilities of diagnosis or treatment of cancer.

2.4. Patient data security

The registry database is maintained in an inaccessible network, with no connection to the internet. The database files are encrypted and accessible only by password. The registry premises are not accessible to unauthorised personnel; completed registration forms are kept in a

locked cabinet. The registry data are saved monthly to an encrypted external disk.

The registry operation is under the authority of the Advisory Committee on Management of Health Research Information and the National Non-Communicable Disease Control Program of the Ministry of Health of Benin.

2.5. Data analysis

Incidence rates are calculated based on all malignant invasive cancers. The data are processed and analysed using the software R. The frequency and incidence tables are produced using the CanReg 5 software, and Excel 2010[®].

The results are presented as the number of cases recorded, crude, age standardised (ASR) and cumulative (0–74) incidence rates for a period of 3 years (2014–2016). Age standardisation was carried out by the direct method, using the world standard population [9].

3. Results

In the three-year period (2014–2016) a total of 1086 cases of cancer (ICD -10 codes: C00-C96) were registered among Cotonou residents, 608 cases (56.0%) among women, corresponding to an age-standardized incidence rate of 78.4 per 100,000 person-years, and 478 (44.0%) among men corresponding to an age-standardized incidence rate of 91.8 per 100,000 (Table 1).

Overall (both sexes) some 3.5% of cancer cases ($n = 38$) occurred in childhood (ages 0–14), and 16% in the elderly (ages 70 or more), but the age distribution was very different by sex, with females being, on average younger at the time of diagnosis (48.5, compared with 54.2 in males). 37.7% of cancers in women were in the age group 30–49 years at diagnosis compared to 24.7% for men. 23.2% of men with cancer were over 70 years of age compared to 10.4% of women.

Table 1 shows the numbers of cases, crude and age standardised and cumulative incidence rates by cancer type (classified by ICD-10) in males and females. The percentage of cases – by cancer site – diagnosed on the basis of morphology (histology or cytology) is also shown.

Prostate cancer (C61) was the most commonly diagnosed cancer among men, comprising 23.2% of all cases, with an age-standardized rate of 30.5 per 100,000. The next most frequent, in terms of numbers of cases, were liver cancers (11.1%) and large bowel cancers (C18-20) (8.6%), leukaemias (7%) and stomach cancer (6.1%). In women breast cancer (C50) was the most common cancer accounting for 32.1% of all cases, with an age-standardized incidence rate of 22.6 per 100,000. Cancer of the cervix uteri (C53) ranked second (17.1%), with an age-standardized incidence 14.9 per 100,000. These two cancers comprised almost half of all female cancers.

Fig. 2 shows, on a semi-logarithmic scale, the age-specific incidence rates of the four most common cancers: liver, prostate, breast and cervix. In men, prostate cancer shows a rapid and progressive rise in incidence from the 50–54 age group. In women, breast cancer begins at a much younger age (20–24 years) with a steady rise and relatively little change in incidence after the age of peak in the 50–54. The increase in cervical cancer starts at an older age (30–34) than breast cancer, and the incidence shows a rather steady increase with age, so that, the mean age at diagnosis (55.0) is seven years later than for breast cancers (47.6).

4. Discussion

Until 2013, there were no population-based data on the cancer profile in Benin. The only published data were based on histology reports from the department of pathology in Cotonou of cases referred from gynaecology in 2000–2008 [10,11]. The national estimate for Benin in Globocan 2012 [12] was derived from the average incidence of cancer (all sites) in West Africa, partitioned according to the relative

Table 1
Numbers of cases recorded by site and sex incidence rates and percentage of microscopic verification (MV%) of diagnosis: Cotonou (2014–2016).

ICD-10	Males							Females						
	No.	%	MV%	Incidence			No.	%	MV%	Incidence				
				Crude (per 10,000)	ASR (per 10,000)	Cumulative (0-74) %				Crude (per 10,000)	ASR (per 10,000)	Cumulative (0-74) %		
Oral cavity & pharynx	C00-C14	26	5.4	57.7	2.5	3.6	0.39	24	3.9	54.2	2.1	3.3	0.44	
Oesophagus	C15	24	5.0	75	2.3	5.5	0.75	15	2.5	66.7	1.3	2.6	0.32	
Stomach	C16	29	6.1	62.1	2.8	5.4	0.64	17	2.8	82.4	1.5	2.4	0.26	
Colon& Rectum	C18-20	40	8.6	77.6	3.9	7.3	0.97	22	3.7	68	1.9	3.0	0.30	
Liver	C22	53	11.1	11.3	5.2	7.9	0.84	19	3.1	5.3	1.7	2.9	0.32	
Pancreas	C25	11	2.3	27.3	1.1	1.8	0.22	14	2.3	0	1.2	2.3	0.33	
Lung	C33, C34	7	1.5	42.7	0.7	1.3	0.13	6	1	66.7	0.5	0.9	0.15	
Skin (excl melanoma)	C44	18	3.7	61.1	1.6	2.7	0.26	16	2.6	64.7	1.2	1.7	0.19	
Breast	C50							195	32.1	74.4	17.2	22.6	2.31	
Cervix	C53							104	17.1	84.6	9.2	14.9	1.68	
Corpus uteri	C54-55							23	3.8	87	1.8	3.7	0.64	
Ovary	C56							22	3.6	54.5	1.9	0.3	2.7	
Prostate	C61	111	23.2	51.1	10.9	30.5	3.30							
Kidney	C64	12	2.5	75	1.2	2.0	0.28	10	1.6	20	0.9	1.2	0.12	
Bladder	C67	12	2.5	8.3	1.2	2.2	0.35	3	0.5	66.7	0.3	0.4	0.03	
Eye	C69	2	0.4	100	0.2	0.4	0.08	12	2	66.7	1.1	1.1	0.07	
Brain & Nervous syst.	C70-72	11	2.3	18.2	1.1	1.9	0.33	7	1.2	28.6	0.6	0.7	0.06	
Thyroid	C73	0	0	100	0	0	0	7	1.2	100	0.6	0.9	0.07	
Lymphomas	C81-85	18	3.8	88.9	1.8	2.2	0.23	12	2.0	68.8	1.1	1.1	0.08	
Leukaemia	91-95	33	7.0	100	3.2	5.1	0.41	27	4.4	100	2.4	3.3	0.38	
Other and non specific		71	13.0		10.9	30.5	3.30	53	8.1					
All sites		478	100	57.0	46.7	91.8	10.42	608	100	71.0	53.5	78.4	8.78	

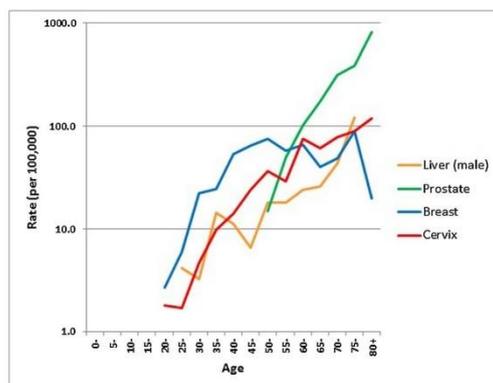


Fig. 2. Age-specific incidence rates (per 100,000) for the four most common cancers in Cotonou 2014–2016.

frequency of different cancers in unpublished data from two pathology departments. It suggested an ASR of 87.2 per 105 in males, with the most common cancers being liver (22.9%), prostate (21.5%) and colon-rectum (6.6%); the ASR in females was 102.7 per 100,000, with more than half of the cases being cancers of the breast (30%) or cervix (26%). Apart from the rather more frequent occurrence of prostate cancer and the lower frequency of liver cancer in males, and lower than predicted rates in females, the incidence data from Cotonou for 2014–6 are rather similar, and these were used for the more recent national estimates in Globocan 2018 [1].

Although most of the cases registered (56%) represent patients diagnosed and treated in the major teaching hospital (National University Hospital (CNHU)), a substantial proportion (43% of cases in males, 29% in females) were registered without a histological confirmation of

diagnosis. This is in part because of the low proportion of histological diagnosis of liver cancers (less than 10% of cases (Table 1) are histologically verified). The data obtained are subject to checks for duplicate registrations, and validity of recorded information by the CanReg software [13]. The lack of comprehensive registration of deaths means that death certificates cannot be used as a source of information by the registry, nor for appraisal of completeness of case finding. The registration of cases not diagnosed through pathology implies lack of validity concerning the precise cancer diagnosis, but is generally reassuring concerning the thoroughness of case finding in a registry [14], although the low overall incidence in women, compared with the regional average (cumulative rate 8.8% in Cotonou vs 13.6% in West Africa [1]) suggests otherwise.

Fig. 3 compares cumulative incidence rates in Cotonou with other regional registries, and with the black population of the USA. In general, the rates in males are rather similar to those in other regional registries, while the rates for cancers of females – especially cervix cancer, are rather lower (although the latter is still more than double the rate observed in the black population of the USA). The pathology series cited above [11] had suggested that breast cancer was more common than cervix cancer (93 and 56 cases, respectively, in 9 years), although it was pointed out that the probability of biopsy in case of advanced cervix cancer was lower than for breast cancer cases of similar stage. In the present population-based data, the proportion of registered cases with histology is higher for cervix (85%) than breast cancer (74%), which may imply a degree of under-registration of this cancer [14]. There is no systematic screening programme for cancer of the cervix in Benin, and no cases of carcinoma in situ registered in the 3-year period.

In 2012, the prevalence of HIV infection among adults (15–49) in Cotonou was reported to be 1.9% [15]. A regional study has shown the risk of Kaposi sarcoma to be greatly increased by HIV infection [16], despite which cases of Kaposi sarcoma were very rare (no cases in women, and only 3 cases in men – all above age 45).

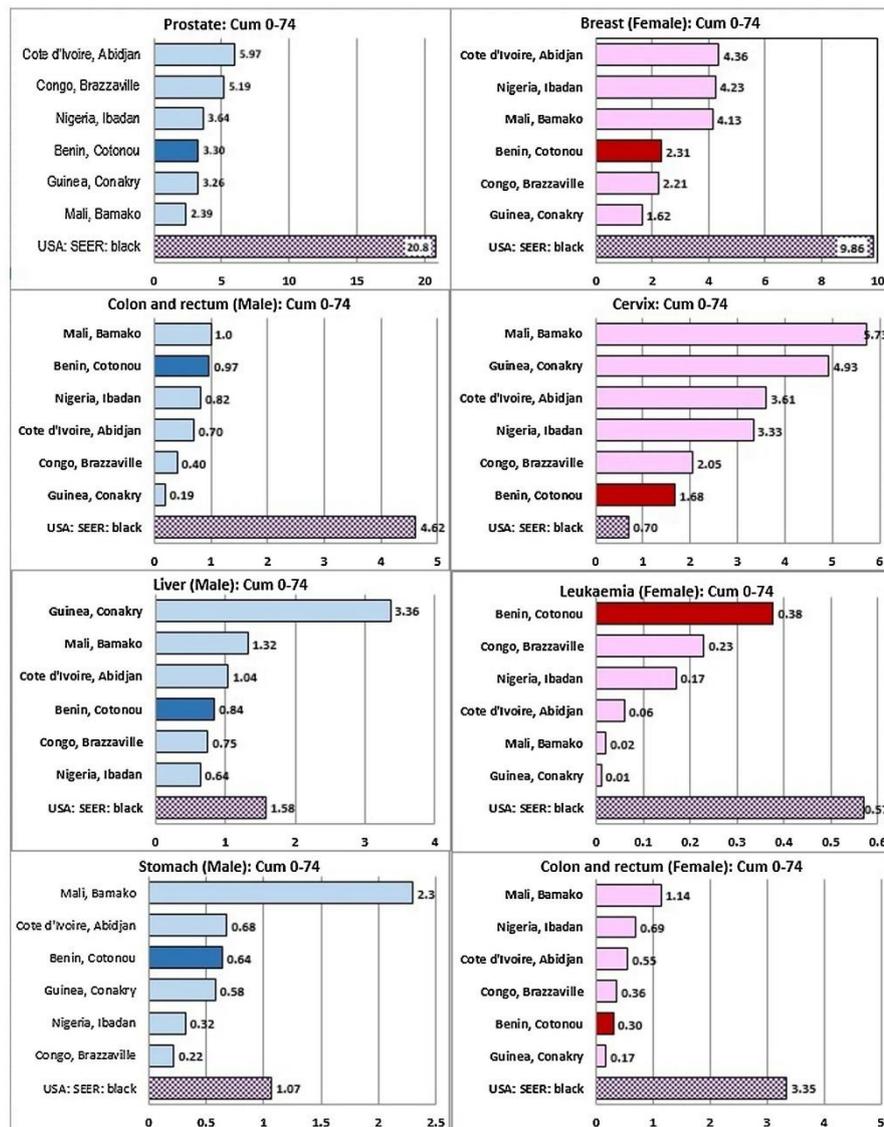


Fig. 3. Comparison of incidence rates (cumulative rate (0–74) %) of the four most common cancers in each sex, with rates in other regional cancer registries and in the black population of the US SEER registries, 2008–2012 (source [13]). Other regional cancer registries and the years concerned: Congo, Brazzaville 2009–13; Cote d'Ivoire, Abidjan 2014–15; Guinea, Conakry 2001–10; Mali, Bamako 2010–14; Nigeria, Ibadan 2006–09 (source [17]).

5. Conclusion

As in West Africa as a whole, four cancers dominate in Cotonou: prostate and liver cancers in men (one third of male cancers) and breast and cervix cancer in women (almost 50% of female cancers), underlining the need for programmes of early detection to improve outcome (breast and prostate), and for prevention of liver and cervix cancer through vaccination, and cervix cancer by screening. The establishment

of a cancer registry in Benin is part of the National System of Information and Sanitary Management (SNIGS) of Non-communicable Diseases (NCDs). The epidemiological surveillance of cancers in Benin has been partly ensured by the establishment of the Cotonou Cancer Registry, which covers about 10% of Benin's population.

The Cotonou Cancer Registry is scientifically and technically supported by the PNLMT of the Ministry of Health of Benin.

Despite its small size (only 10% of the national population resulting

in a relatively small number of enrolments), the Cotonou Cancer Authority is expected to provide vital information for the planning and evaluation of cancer control programs. To improve the completeness of the registration of cases, the registry has intensified its efforts to collect data on eligible cases of cancer diagnosed in outpatient clinics / hospitals in the city of Cotonou.

Conflicts of interest

The authors declare no conflict of interest.

Contributions of the authors

- Mr Marcel D. EGUE : Ensured the collection and analysis of data. He prepared the first draft of this article and participated in the writing.
- Dr. Freddy H.R. GNANGNON : participated in the discussion of the results and the writing of the article.
- Prof. Marie-Thérèse AKELE AKPO: Conception and design of the cancer registry. Participated in the discussion of the results and to the editor of the article.
- Dr. Max PARKIN : has helped in the discussion of the results, the drafting and translation of the article and its publication in a scientific journal.

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I.1.2. Mortalité

Le cancer du sein est la première cause de mortalité par cancer dans 110 des 185 pays couverts par l'observatoire GLOBOCAN du CIRC (**Figure 3**). Le cancer du sein est précédé par le cancer du poumon en Australie/Nouvelle-Zélande, en Europe du Nord, en Amérique du Nord et en Chine et par le cancer du col de l'utérus dans de nombreux pays d'ASS (Bray et al., 2024).

Il est également la principale cause de mortalité par cancer chez les femmes dans le monde. Selon l'OMS, en 2020 environ 685 000 décès dus au cancer du sein ont été enregistrés dans le monde soit un décès par cancer sur 6 chez la femme (Bray et al., 2024).

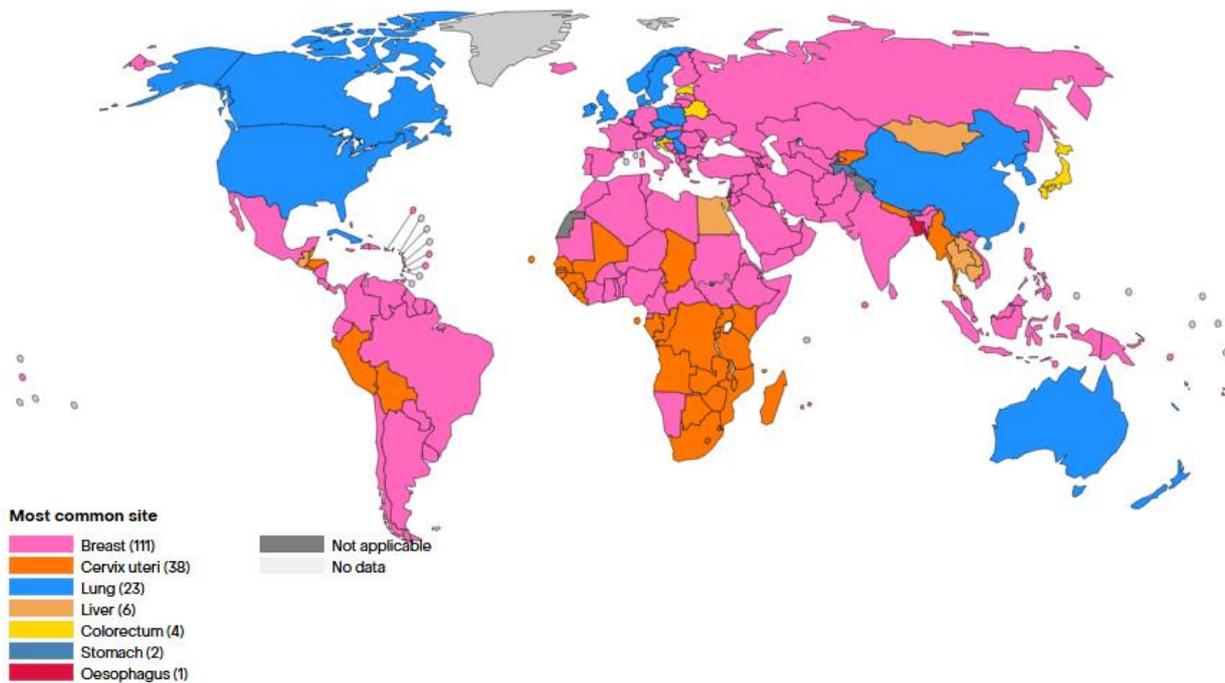


Figure 3: Répartition des pays en fonction de la première cause de mortalité par cancer chez la femme (GLOBOCAN, 2022)

Comme l'incidence, la mortalité liée au cancer du sein varie sensiblement d'une région géographique à une autre mais la tendance semble être l'inverse de celle observée pour l'incidence. Par exemple bien que l'incidence soit la plus faible en ASS, la mortalité y est la plus élevée. Les taux de mortalité les plus élevés sont donc observés en Mélanésie, en Afrique de l'Ouest, en Micronésie/Polynésie et dans les Caraïbes. La Barbade ayant le taux de mortalité le plus élevé au monde (Sung et al., 2022). Ainsi les femmes vivant dans les pays à revenu faible et intermédiaire



ont des taux de mortalité jusqu'à 17% plus élevés que les femmes des pays développés (15,0 et 12,8 pour 100 000, respectivement) (**Figure 4**).

En outre, 70 % des décès liés au cancer du sein surviennent dans les pays à revenu faible et intermédiaire, ce qui fait peser un fardeau important de mortalité dans ces régions (Lukong et al., 2017). Cette disparité s'explique par le fait que les pays situés dans des régions historiquement à haut risque (pays à index de développement élevé) ont le plus bénéficié des progrès réalisés grâce à plusieurs percées dans le domaine du dépistage et des traitements efficaces. Les taux de mortalité ayant diminué dans ces pays depuis la fin des années 1980 et le début des années 1990 (Sung et al., 2022). Parallèlement, dans les pays à revenu faible et intermédiaire, en raison du manque d'accès aux services de dépistage et aux traitements appropriés, la maladie est souvent diagnostiquée à des stades avancés, réduisant ainsi les chances de survie (Gnangnon et al., 2021).

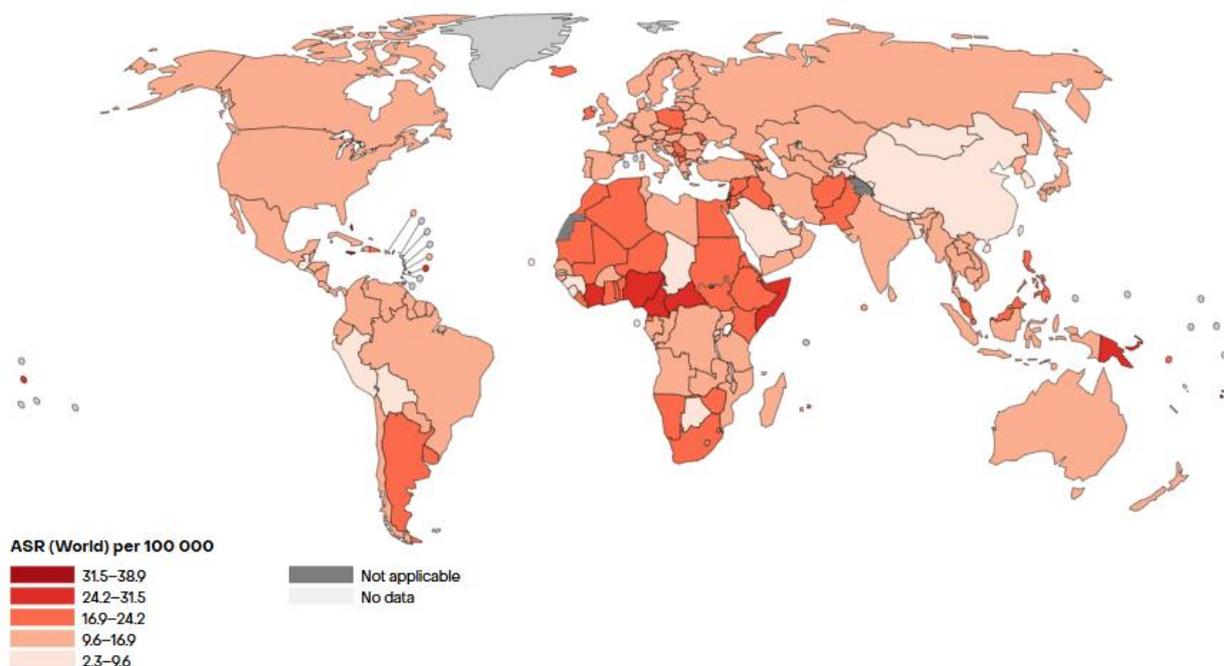


Figure 4: Taux de mortalité standardisés du cancer du sein dans le monde (GLOBOCAN, 2022).

I.1.3. Facteurs de risque

Plusieurs facteurs de risque ont été identifiés comme pouvant influencer la survenue et le développement du cancer du sein chez la femme.

I.1.3.1. L'âge

L'âge est un puissant facteur de risque du cancer du sein. Plus de 80% des cancers du sein sont diagnostiqués après l'âge de 50 ans (Kamińska et al., 2015) ; de plus le risque croît avec l'âge des patientes (Rojas & Stuckey, 2016 ; Sancho-Garnier & Colonna, 2019). Moins de 5 % des cancers du sein surviendraient chez des femmes de moins de 40 ans (Rojas & Stuckey, 2016).

I.1.3.2. Les facteurs hormonaux

Les principaux facteurs hormonaux sont :

- **La longue vie génitale : Age aux ménarches précoce (< 12-13 ans) et ménopause tardive**

En effet, un âge précoce aux premières règles correspond à une exposition précoce et très souvent prolongée à l'imprégnation hormonale notamment oestrogénique endogène (Sancho-Garnier & Colonna, 2019). Ainsi, le risque de cancer du sein en pré-ménopause est réduit de 9 % pour chaque année d'âge où les ménarches sont retardées (Rojas & Stuckey, 2016).

Parallèlement, les femmes qui ont leur ménopause après 55 ans présentent un risque accru de cancer du sein, en comparaison avec celles dont les menstruations cessent précocement (Sancho-Garnier & Colonna, 2019).

- **La contraception orale oestroprogestative**

Il existe une liaison évidente entre usage de contraceptifs oestroprogestatifs et le risque de cancer du sein. Ce risque est augmenté d'environ 25 % chez les femmes utilisant couramment les contraceptifs oraux. Un risque relatif de l'ordre de 1,5 est notamment retrouvé pour les femmes ayant utilisé des contraceptifs oraux très jeunes pendant au moins 5 ans et avant une première grossesse (Sancho-Garnier & Colonna, 2019).

- **L'utilisation d'un traitement hormonal de la ménopause**

Le traitement hormonal substitutif (THS) de la ménopause par une association oestroprogestative multiplie le risque des cancers du sein post-ménopausiques de 1,1 à 2,1. Le risque augmente avec la durée de l'utilisation du traitement. Ce constat explique la forte diminution de la prescription de THS dans les pays occidentaux comme la France (Nyante et al., 2013; Sancho-Garnier & Colonna, 2019; Writing Group for the Women's Health Initiative Investigators, 2002).

I.1.3.3. Les facteurs liés à la reproduction

- **La nulliparité**

C'est l'un des premiers facteurs de risque du cancer du sein, identifié. Comparées aux femmes n'ayant pas eu d'enfants, les femmes qui ont eu au moins une grossesse à terme, ont en moyenne une réduction de risque de cancer du sein de 25 %. La protection semble augmenter avec le nombre d'enfants (Rojas & Stuckey, 2016).

- **Première grossesse tardive** (Colditz, 2000 ; Layde et al., 1989)

Les femmes ayant un premier enfant après l'âge de 30 ans ont un risque plus élevé, et le risque augmente avec l'âge tardif de la première grossesse pour atteindre un ordre de grandeur de 3 à 4, après 38 ans (Nyante et al., 2013 ; Sancho-Garnier & Colonna, 2019). La tendance actuelle, avec



l'occidentalisation du mode de vie observée en ASS, est responsable du recul de l'âge des femmes à la première grossesse et pourrait expliquer l'augmentation de l'incidence du cancer du sein sur le continent africain. Une explication de l'effet protecteur de la première grossesse précoce est que celle-ci induirait une différenciation terminale des glandes mammaires les rendant moins sensibles aux divers carcinogènes (Sancho-Garnier & Colonna, 2019).

- **L'allaitement**

Il existerait un effet protecteur de l'allaitement prolongé, avec une diminution du risque de 4% par année d'allaitement (Eliassen et al., 2006). Cet effet protecteur de l'allaitement, pourrait être dû à la sécrétion de prolactine et/ou de périodes anovulatoires avec une réduction de la sécrétion d'oestrogène et est surtout retrouvé dans les études réalisées dans les pays en développement (Sancho-Garnier & Colonna, 2019).

I.1.3.4. Les facteurs génétiques et familiaux

- **Histoire familiale de cancer du sein :**

Un antécédent familial au premier ou au second degré augmente le risque de cancer du sein et est retrouvé chez 10 à 15% des patientes (Sancho-Garnier & Colonna, 2019). Ce risque est influencé aussi bien par le degré de parenté que le nombre de parents atteints. Il est multiplié par près de 2 si un seul parent au premier degré est atteint ; et par près de 3 si deux parents sont touchés par la maladie. Ce risque est d'autant plus élevé que l'âge au diagnostic du parent de 1er degré atteint est précoce (« Familial Breast Cancer », 2001)

- **Mutations génétiques héréditaires :**

Elles augmentent fortement le risque de cancer du sein. Les mutations les plus étudiées et les plus importantes sont celles liées aux gènes BRCA1 et BRCA2. Ces mutations représentent environ 80% des cancers du sein héréditaires et 5 à 6% de tous les cancers du sein (Greene, 1997), et sont identifiées dans la moitié des cas familiaux. Une mutation BRCA est associée à un risque de 55 à 80% de développer un cancer au cours de la vie (Sancho-Garnier & Colonna, 2019).

I.1.3.5. Les maladies bénignes du sein

Les maladies bénignes du sein constituent un facteur de risque de cancer du sein. Elles sont histologiquement divisées en deux groupes : les lésions prolifératives et les lésions non prolifératives avec ou sans atypie. Les lésions non prolifératives ne sont généralement pas associées à un risque accru de cancer du sein ou, si elles le sont, le risque est très faible. Les lésions

prolifératives sans atypie multiplient le risque par deux, tandis que les lésions hyperplasiques avec atypie multiplient ce risque par au moins quatre (Nkondjock & Ghadirian, 2005). Par contre, le fibroadénome isolé ne semble pas constituer un facteur de risque. L'augmentation de la densité mammaire à l'imagerie est également un facteur de risque de cancer du sein (Sancho-Garnier & Colonna, 2019).

I.1.3.6. Les caractéristiques statur pondérales, la nutrition

- **Le surpoids et l'obésité**

Le surpoids et l'obésité à l'âge adulte sont des facteurs de risque pour le cancer du sein post-ménopausiques (RR : 1,2 à 2,5), mais cette association est inconstamment retrouvée pour le cancer du sein survenant avant la ménopause (Key et al., 2001; Lee et al., 2019). Des études récentes ont montré une liaison entre le poids et la taille à la naissance et le risque de cancer du sein avant la ménopause. Ainsi une taille à la naissance supérieure à 53 cm serait associée à un risque de l'ordre de 1,8 par rapport aux femmes nées avec une taille inférieure à 50 cm. Des constats similaires ont été faits pour le poids de naissance avec un risque relatif de 1,5 pour un poids de naissance supérieurs à 3 840 g par rapport à des poids inférieurs à 3040 g (Sancho-Garnier & Colonna, 2019).

- **Consommation d'alcool**

Le rôle de l'alcool est considéré comme convaincant dans les cancers du sein post ménopausique et probable pour les cancers pré-ménopausiques (Sancho-Garnier & Colonna, 2019). La relation entre la consommation quotidienne moyenne d'alcool et le risque de cancer du sein est exponentielle (Steward & Wild, 2014) (**Figure 5**).

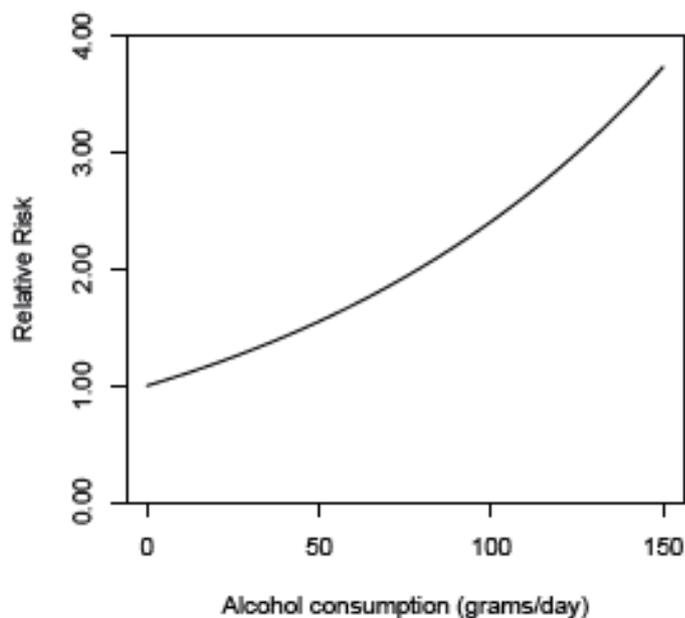


Figure 5: Risque relatif de développer un cancer du sein en fonction de la consommation journalière d'alcool (Steward & Wild,2014)

- **L'activité physique**

Les femmes ayant une activité physique modérée régulière ont un risque plus bas de cancer du sein par rapport aux femmes sédentaires (Sancho-Garnier & Colonna, 2019). Cet effet protecteur est optimal lorsque l'activité physique est régulière et pratiquée entre 35 et 50 ans, est plus important pour les femmes de petits poids et augmente avec l'importance de l'exercice physique (Sancho-Garnier & Colonna, 2019).

I.1.3.7. Rayonnements ionisants

Les femmes ayant été exposées à des radiations ionisantes de la région thoracique notamment avant l'âge de 20 ans (catastrophe nucléaire d'Hiroshima et de Nagasaki, surveillance radiologique d'une tuberculose pulmonaire au début du 20^{ème} siècle), ont un risque augmenté de cancer du sein comme en témoigne les études historiques. Les mammographies répétées pourraient également augmenter le risque de cancer du sein chez les femmes ayant eu des mammographies régulièrement à partir de 30 ans (Sancho-Garnier & Colonna, 2019).

I.1.3.8. Tabagisme

Le risque semble probable aussi bien pour le tabagisme actif que pour le tabagisme passif.

Le risque associé au tabagisme passif est en moyenne de 1,27 et jusqu'à 1,68 pour les cancers du sein pré-ménopausiques.

En ce qui concerne le tabagisme actif, le risque de cancers pré- et post-ménopausiques est de 1,46, augmentant jusqu'à 1,75 pour les femmes ayant commencé à fumer dans les 5 ans suivant la puberté. Avec la prévalence croissante du tabagisme chez les femmes dans de nombreux pays du monde et d'ASS, le nombre de cas attribuables à ce facteur peut ne pas être négligeable. De plus, le sevrage tabagique chez les patientes atteintes de cancer du sein réduit la mortalité (Sancho-Garnier & Colonna, 2019; Travade et al., 2001).

I.1.4. Facteurs pronostiques

I.1.4.1. L'âge au diagnostic

De nombreux travaux empiriques accordent une importante place à l'âge au moment du diagnostic parmi les facteurs pronostiques des décès causés par le cancer du sein. Tsuchiya et al. (Tsuchiya et al., 1997) montrent que le jeune âge au début du cancer est un facteur pronostique indépendant. Dans le même sens, une étude menée par Bonnier et al. (Bonnier et al., 1995) révèle que l'âge de moins de 35 ans est un facteur de risque indépendant. Dans la même perspective, l'étude de Jauffret et al. (Jauffret et al., 2015) montre une mortalité plus élevée chez les femmes de moins de 50 ans.

I.1.4.2. Le stade au diagnostic

Dans leur étude, (Ben Gobrane et al., 2007) font ressortir que la taille de la tumeur, l'extension ganglionnaire, la présence de métastase font partie des facteurs pronostiques des décès associés au cancer du sein. Dans la même perspective, à travers leur étude sur les facteurs pronostiques de la survie au cancer du sein en République islamique d'Iran, (Nematolahi et al., 2018) montrent que la mortalité par cancer du sein est influencée par le statut ganglionnaire et la taille de la tumeur. Selon (Donegan, 1997), la présence ou l'absence de métastases est le prédicteur le plus influent du décès après le traitement du cancer du sein. En effet, en l'absence de traitement adjuvant systématique, le risque de récurrence dans les 10 ans est de 24 % pour les patientes sans métastase ganglionnaire à l'examen histologique, tandis qu'il est de 76 % pour les patientes avec métastase ganglionnaire.

Ces résultats concordent en soulignant le rôle du stade au diagnostic comme facteur pronostique du cancer du sein. Ainsi il y a moins de risques de récurrence lorsque le cancer du sein est diagnostiqué à un stade précoce. En revanche, lorsque le diagnostic est effectué à un stade avancé, le pronostic est moins favorable. Grosclaude et al. dans une étude retrouvent l'influence du stade comme un facteur pronostique indépendant. En effet, les taux de survie relative à 5 ans sont respectivement de 97%, 91 %, 82 % et 29 % pour les stades I, II, III, IV ; plus le stade est élevé plus le risque de décès de la femme est élevé (Grosclaude et al., 2001). Dans leur modélisation multi-états, Broët et al. (Broët et al., 1999) montrent également que le stade clinique élevé est associé à un risque accru de décès.

I.1.4.3. Les sous-types moléculaires de cancer du sein

Le cancer du sein est une maladie très hétérogène dont le traitement et le pronostic varient considérablement d'une patiente à l'autre. La conférence internationale de St. Gallen a permis de définir une nouvelle classification des sous-types moléculaires de cancer du sein (triple négatif, luminal A, luminal B, HER2, etc).

Le cancer du sein triple négatif (CSTN) est un type invasif et de mauvais pronostic en comparaison aux autres types. Sa mortalité est estimée à 40 % au cours des 5 premières années suivant le diagnostic et environ 46% des patientes présenteront des métastases à distance (Yin et al., 2020).



I.2. Prise en charge du cancer du sein en ASS et au Bénin

Il existe peu de données sur la thérapie réellement reçue par les femmes et l'impact de ce traitement sur la survie. A titre d'illustration de ce paragraphe, nous avons contribué (pages suivantes) à une étude qui avait pour but de décrire le traitement anticancéreux reçu par les patientes atteintes d'un cancer du sein en population générale en ASS, de comparer ces thérapeutiques avec les directives harmonisées du NCCN (National Comprehensive Cancer Network) pour l'ASS et d'évaluer l'impact sur la survie.

Un échantillonnage aléatoire de patientes atteintes de cancer du sein prises en charge entre 2009 et 2015, a été effectué dans 11 registres du cancer basés sur la population de 10 pays d'ASS (Bénin, Congo, Côte d'Ivoire, Éthiopie, Kenya, Mali, Mozambique, Namibie, Ouganda et Zimbabwe). Des méthodes actives ont été utilisées pour retracer ces patientes et mettre à jour les données sur le traitement et la survie.

Parmi les 809 patientes incluses, 517 (63,8 %) ont pu être retracées, cette proportion variant selon les pays. Seulement une patiente retracée sur cinq répondait aux critères diagnostiques minimaux (stade du cancer et statut des récepteurs hormonaux connus) pour l'utilisation des directives harmonisées du NCCN (Abulkhair et al., 2010). Le statut des récepteurs hormonaux était inconnu pour 72,5 % des patientes. Parmi les patientes retracées atteintes d'un cancer du sein non métastatique (stade I à III soit n=320), 50,9 % ont reçu un traitement inadéquat selon les recommandations du NCCN ou n'ont pas du tout reçu de traitement anticancéreux.

Cette étude a permis de montrer que l'instauration d'un traitement adéquat et le diagnostic à un stade précoce ont été les principaux déterminants de la survie. Par conséquent, la détection précoce du cancer du sein et un meilleur accès aux méthodes diagnostiques et thérapeutiques est nécessaire pour améliorer l'adhérence aux recommandations et la survie.

Breast Cancer Diagnostics, Therapy, and Outcomes in Sub-Saharan Africa: A Population-Based Registry Study

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ABSTRACT

Background: Breast cancer (BC) is the most common cancer in sub-Saharan Africa (SSA). However, little is known about the actual therapy received by women with BC and their survival outcome at the population level in SSA. This study aims to describe the cancer-directed therapy received by patients with BC at the population level in SSA, compare these results with the NCCN Harmonized Guidelines for SSA (NCCN Harmonized Guidelines), and evaluate the impact on survival. **Methods:** Random samples of patients with BC (≥ 40 patients per registry), diagnosed from 2009 through 2015, were drawn from 11 urban population-based cancer registries from 10 countries (Benin, Congo, Cote d'Ivoire, Ethiopia, Kenya, Mali, Mozambique, Namibia, Uganda, and Zimbabwe). Active methods were used to update the therapy and outcome data of diagnosed patients ("traced patients"). Excess hazards of death by therapy use were modeled in a relative survival context. **Results:** A total of 809 patients were included. Additional information was traced for 517 patients (63.8%), and this proportion varied by registry. One in 5 traced patients met the minimum diagnostic criteria (cancer stage and hormone receptor status known) for use of the NCCN Harmonized Guidelines. The hormone receptor status was unknown for 72.5% of patients. Of the traced patients with stage I–III BC ($n=320$), 50.9% received inadequate or no cancer-directed therapy. Access to therapy differed by registry area. Initiation of adequate therapy and early-stage diagnosis were the most important determinants of survival. **Conclusions:** Downstaging BC and improving access to diagnostics and care are necessary steps to increase guideline adherence and improve survival for women in SSA. It will also be important to strengthen health systems and facilities for data management in SSA to facilitate patient follow-up and disease surveillance.

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Background

Breast cancer (BC) is the most common cancer among women in sub-Saharan Africa (SSA) and is the second leading cause of cancer death after cervical cancer.¹ Approximately 7 in 10 women diagnosed in SSA present with advanced stages of disease (stages III–IV).² Survival among these patients is relatively poor; however, there are survival differences between African countries.^{3–6}

BC treatment is resource-intensive. For nonmetastatic BC, the main pillars of therapy are surgery, radiotherapy (RT), chemotherapy, endocrine therapy (if hormone receptor-positive), and targeted therapies. In SSA, all of these recommended treatment modalities are available in only a few state-of-the-art cancer facilities. Typically, accessibility to such institutions is limited to residents of these areas, those who are covered by health insurance schemes, or those who can afford to pay out-of-pocket. Few African nations have country-specific treatment recommendations, and most often, clinicians offer therapy options based on available local resources. NCCN developed resource-stratified therapy recommendations for

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SSA for the most common cancers⁷ to facilitate therapeutic decision-making for clinicians in resource-constrained settings. There is limited information, however, on whether BC therapy in SSA is concordant with these resource-stratified therapy recommendations.

Most information on BC therapy and survival in SSA is from hospital-based reports, and these describe the survival of patients treated in cancer referral centers. Although these patients receive the best therapy locally available, survival is generally poor. However, what is not known is the experience of the general population of patients with BC in different SSA countries (not only those reaching specialist treatment centers) by way of the therapy received and how this influences survival. To address this knowledge gap, we performed this study including random samples of women from 11 population-based cancer registries (PBCRs) in SSA to describe the cancer-directed therapy (CDT) received at the population level, compare these results to recommended guidelines, and evaluate the impact on survival.

Methods

Study Design, Population, and Data Source

This was a retrospective population-based registry study. The sampling frame was the database of the African Cancer Registry Network (AFCRN).⁸ After excluding patients registered based on a death certificate only, we drew random samples of at least 40 patients with BC (per ICD-10, code C50) per registry of patients diagnosed from 2009 to 2015 from 10 PBCRs: Abidjan (Côte d'Ivoire), Bamako (Mali), Brazzaville (Congo), Bulawayo (Zimbabwe), Cotonou (Benin), Eldoret (Kenya), Kampala (Uganda), Maputo (Mozambique), Namibia, and Nairobi (Kenya). In Addis Ababa (Ethiopia), we included all patients diagnosed from January to March 2012. All included patients were African women who were residents of the registry area. The number of randomly selected patients per registry was determined by the practical feasibility of retrospectively tracing health records across multiple centers. All of these PBCRs cover a city, except for the Namibian cancer registry, which covers the national territory. All the registries use the CANREG software developed by the International Agency for Research on Cancer for data entry and for verification checks. Records were traced from the registry to the source of registration, and information on the date of diagnosis and stage was verified or updated and any duplicates excluded (see supplemental eFigure 1, available with this article at JNCCN.org). The registry records were updated with information on diagnostic procedures, treatment received, and patients' vital status from clinical records. However, if this information could not be found in clinical records, then as a last resort the

patients or relatives were contacted by registry staff when a contact number was available.

Patients for whom we succeeded in obtaining additional information that was not routinely available in the registry records, from either the source health facilities and/or from reaching patients or their next of kin, are subsequently referred to as "traced patients."

Data management was conducted using SPSS Statistics, version 25 (IBM Corp) and data analyses were performed with STATA, version 14.2 (StataCorp, LP).

Explanatory and Outcome Measures

The main explanatory variable was the therapy received. The outcome measure was the patients' vital status at the closing date of the study. This measure was ascertained by active follow-up methods as described earlier. The observational time was the time from diagnosis to death, date of last contact, or until the end of the study (December 31, 2017), whichever occurred first. Patients not found to have died, using the active methods as described, were counted as being alive.

Ethical Considerations

This study used anonymized and encrypted data from the AFCRN database. The study protocol was approved by the Research Committee of the AFCRN, by the individual registries, and by the Martin-Luther-University Halle-Wittenberg Review Board (votum number 2019-009). The study complied with the Declaration of Helsinki.

Data Management and Assessing Therapy

We used the NCCN Harmonized Guidelines for Sub-Saharan Africa (NCCN Harmonized Guidelines for SSA) for Breast Cancer, version 2.2017,⁹ as a guide for therapy evaluation. Information on stage at diagnosis, hormone receptor status (HRS), and tumor histology are required to use these guidelines for therapy evaluation effectively. To use the same classification categories as the NCCN Harmonized Guidelines for SSA and based on the anatomic stage groupings of the AJCC, we categorized patients into 3 stage groups for therapy evaluation: early BC (stages I, II, and T3N1M0), locally advanced BC (stage IIIA [except T3N1M0], IIIB, and IIIC), and metastatic disease (stage IV, M1).¹⁰ Patients with early and locally advanced BC are subsequently referred to as "patients with curable or non-metastatic disease."

For chemotherapy, RT, hormonal therapy, surgery, and targeted therapy, we assessed whether there was documented evidence that the patient had initiated treatment. To assess chemotherapy completeness, we evaluated what proportion of patients received the prescribed chemotherapy regimen. We categorized chemotherapy received as >85% complete if the patient received all but one prescribed chemotherapy session, as ≤85% com-

plete¹¹ if the patient had ≥ 2 missed chemotherapy sessions, and unknown if there was no record of chemotherapy found. We were unable to assess the completeness of RT because the total dose received was not recorded for most patients. Completeness of endocrine therapy could not be assessed because we could not ascertain therapy adherence and completion until year 5. For surgery, we categorized patients as having received surgery (either a mastectomy or a lumpectomy) or not.

We used a simplified schema based on these guidelines to evaluate the therapy received. Among traced patients with curable BC, we used the categorization below for therapy evaluation:

1. Initiated adequate therapy (the patient received as a minimum): surgery (mastectomy or [lumpectomy + RT]) and systemic therapy (chemotherapy and/or endocrine therapy) and/or RT
2. Inadequate therapy (with no curative potential): surgery with no systemic therapy, a therapy combination without surgery, or a monotherapy
3. No therapy: traced patients with no evidence of receiving any CDT

For patients with metastatic disease, we described the therapy they received (see Table 1 for therapies).

Assessing Loss to Follow-Up

We assessed the proportion of patients lost to follow-up by registry at year 1, 3, and 5, and used a Cox regression model with loss to follow-up (LTFU) as the outcome, and age and stage at diagnosis as exposure variables to determine whether LTFU was random or associated with either age or stage at diagnosis.

Survival Analyses

For survival analyses, we excluded patients for whom the date of last contact was the same as the date of diagnosis and who thus had no additional follow-up information. We estimated the all-cause Kaplan-Meier survival for patients by therapy received at year 1, 3, and 5, and estimated relative survival by age, stage at diagnosis, therapy modality, and country-level Human Development Index (HDI).

Modeling Excess Mortality

We modeled the excess hazards of death from BC in a framework of generalized linear models using a piecewise Poisson regression model with smoothing splines. We split time into monthly time bands, and adjusted for age, stage at diagnosis, HRS, tumor grade, therapy, and country-level HDI. Registries were grouped by country-level data for parsimony and to improve the power of the multivariable model. All patients with at

least 30 days follow-up and with nonmetastatic BC were included. We estimated the relative excess risk of death from curable BC, after considering background mortality. We obtained data on background mortality from 5-year-age abridged WHO Global Health Observatory life-tables, which we expanded from 5-year ages (eg, ages 0–4, 5–9, and 10–14 years) to single-year ages (eg, ages 0, 1, 2, and 3) using a Poisson regression model with a flexible function. We performed sensitivity analyses limiting the analyses to traced patients and to registries with $<50\%$ LTFU in the first year.

Results

Patient and Tumor Characteristics

A total of 809 patients from 11 PBCRs were included; these patients represented one-fifth of all patients registered with BC during the study period (Table 2). Median age at diagnosis was 48 years. Approximately 16% of the cohort was aged <35 years at diagnosis, with 53% aged <50 years. Additional information on stage, therapy, or vital status was obtained for 63.9% (517 records) of patients using active methods (traced patients), and this proportion varied by registry (Table 2). Half of the registry records were traced to public hospitals, 14.7% were traced to private hospitals, and 35.2% could not be traced to a treatment facility (Table 3). We found that 65.0% of tumors were ductal carcinomas. Of the 809 patients, stage at diagnosis was known for 53.5% ($n=433$; supplemental eFigure 2). Of those with known stage, 20.8% had metastatic disease at time of diagnosis and 46.4% were diagnosed with stage III disease (ie, 67.2% in stages III and IV), with $<2\%$ of patients diagnosed with stage I disease. When limited to the traced patients, stage at diagnosis was known for 405 patients, 320 of whom had nonmetastatic BC.

Regarding imagery for staging, imaging type was recorded in all registries apart from Addis Ababa. Less than 7% of patients had a record of using either a CT scan, an MRI, or bone scintigraphy for staging. Abdominal ultrasounds and chest and bone radiographs were the most commonly used means of screening for metastases. The HRS was recorded for 17.5% of all women and for 27.5% of traced patients.

Therapy Characteristics

Therapy Received and Guideline Adherence

In the population-based cohort, there was no record of any CDT for 48.7% of patients (12.6% of these patients were traced but without any therapy, and 36.1% of records were not traced) (Table 1). Patients from registries in regions with medium HDI (Eldoret, Nairobi, and Namibia) had better access to therapy and/or records of therapy compared with those from registries in regions with low

Table 1. Therapy Characteristics for Patients With BC by Stage at Diagnosis

	Population-Based Cohort n (%)	Traced Cohort (n=517)				
		n (%)	Early-Stage BC ^a %	Locally Advanced BC ^b %	Metastatic BC %	Unknown Stage %
Total, N	809	517	163	153	85	112
Chemotherapy						
Anthracycline-based regimen (without a taxane)	149 (18.4)	149 (28.8)	36.8	26.8	27.1	21.4
Anthracyclines and taxanes	94 (11.6)	94 (18.2)	18.4	25.5	18.8	8.0
Others	41 (5.1)	41 (7.9)	6.1	4.6	10.6	12.5
CMF	5 (0.6)	5 (1.0)	1.8	0.6	0.0	0.9
None recorded	228 (28.2)	228 (44.1)	36.8	42.5	43.5	57.1
Not traced	292 (36.1)	—	—	—	—	—
Neoadjuvant chemotherapy						
Yes	92 (11.4)	92 (17.8)	22.1	22.2	12.9	8.9
None recorded	425 (52.5)	425 (82.2)	77.9	77.8	87.1	91.1
Not traced	292 (36.1)	—	—	—	—	—
Surgery						
Mastectomy	277 (34.2)	277 (53.6)	66.3	57.5	37.6	42.0
Lumpectomy	43 (5.3)	43 (8.3)	10.4	3.3	5.9	14.3
None recorded	197 (24.4)	197 (38.1)	23.3	39.2	56.5	43.7
Not traced	292 (36.1)	—	—	—	—	—
Radiotherapy						
Yes	135 (16.7)	135 (26.1)	28.8	30.1	23.5	19.6
None recorded	382 (47.2)	382 (73.9)	71.2	69.9	76.5	80.4
Not traced	292 (36.1)	—	—	—	—	—
Hormone therapy						
Yes and HR+	74 (9.3)	74 (14.3)	22.7	13.7	7.1	8.9
Yes and HRS unknown	70 (8.6)	70 (13.5)	15.3	13.1	14.1	11.6
Yes and HR-	4 (0.5)	4 (0.8)	0.6	0.0	1.2	1.8
No and HR+	23 (2.7)	23 (4.4)	4.9	4.6	2.3	4.5
No and HR-	41 (5.1)	41 (7.9)	8.6	8.5	12.9	2.7
No and HRS unknown	305 (37.7)	305 (59.0)	47.9	60.1	62.4	70.5
Not traced	292 (36.1)	—	—	—	—	—

(continued on next page)

HDI (Figure 1). There was no statistical association between age at diagnosis and therapy receipt, although there were lower proportions of women who initiated adequate therapy among patients aged 20 to 34 years and ≥ 65 years (supplemental eFigure 3).

When we limited the analyses to the traced cohort (n=517), there was no record of any form of CDT for 19.7% of patients (Table 3). Of these traced patients, 104 (20.1%) had recorded the diagnostic information (stage at diagnosis and HRS) necessary for assessing therapy according to the NCCN Harmonized Guidelines for SSA⁹ (supplemental eFigure 4); the main characteristic unknown was the HRS for 72.5% of traced patients. We

also found that 40.5% of traced patients with early BC and 58.2% of traced patients with locally advanced BC received inadequate therapy with no curative potential or had no record of therapy (Table 1). In total, of all traced patients with curable BC, 50.9% had inadequate or no CDT.

Surgery

Surgery was the most available form of therapy, with a surgical intervention documented for 41% of all women and 64.2% of traced patients (Table 3). Of those who had surgery recorded, 86.6% had a mastectomy. However, the type of mastectomy (simple, modified

Table 1. Therapy Characteristics for Patients With BC by Stage at Diagnosis (cont.)

	Population-Based Cohort n (%)	Traced Cohort (n=517)				
		n (%)	Early-Stage BC ^a %	Locally Advanced BC ^b %	Metastatic BC %	Unknown Stage %
Targeted therapy						
Yes and HER2+	8 (1)	8 (1.5)	2.4	0.7	2.3	0.9
No and HER2+	35 (4.3)	35 (6.8)	11.7	3.9	9.4	1.8
No and HER2-	87 (10.7)	87 (16.8)	20.9	19.6	7.1	14.3
No and HER2 status unknown	387 (47.8)	387 (74.9)	65.0	75.8	81.2	83.0
Not traced	292 (36.1)	—	—	—	—	—
All CDT received						
Surgery + systemic therapy ± radiotherapy	234 (28.9)	234 (45.3)	59.5	41.8	36.5	36.6
Surgery without systemic therapy/monotherapies/therapy combination without surgery	181 (22.4)	181 (35.0)	27.0	39.2	42.3	34.8
No therapy	102 (12.6)	102 (19.7)	13.5	19.0	21.2	28.6
Not traced	292 (36.1)	—	—	—	—	—

Stages classified for therapy assessment following the NCCN Harmonized Guidelines for Sub-Saharan Africa for Breast Cancer⁹ recommendations. For 4 patients the stage at diagnosis was recorded as stage III, without additional details, and thus could not be dichotomized for this table and was not included. Abbreviations: BC, breast cancer; CDT, cancer-directed therapy; CMF, cyclophosphamide/methotrexate/5-fluorouracil; HR, hormone receptor; HRS, hormone receptor status.

^aStages I, II, T3N1M0.

^bStage IIIA apart from T3N1M0, IIIB, IIIC.

radical, or radical) was not always specified, and neither were details on surgical axillary node staging and dissection.

Systemic Therapy

We found that 55.9% of traced patients had a record of chemotherapy (Table 3). Of those, 51.6% had an anthracycline-based regimen, 32.5% had an anthracycline regimen with a taxane, and the others received different combinations of drugs.

In addition, 28.6% of traced patients received endocrine therapy (Table 3). In the traced cohort, 13.5% of patients with tumors of unknown receptor status received endocrine therapy (Table 1). However, 4.4% of patients who had hormone receptor-positive disease had no record of receiving endocrine therapy. More patients diagnosed at early stages of disease had a record of receiving endocrine therapy (Table 1).

Radiotherapy

Approximately 1 in 4 traced patients received RT as part of their treatment regimen (Table 1). The proportion of patients who received RT varied by registry.

Targeted Therapy

Of traced patients, 35 (6.8%) who had HER2-positive disease received no therapy with monoclonal antibodies,

such as trastuzumab (Table 1). Use of trastuzumab was recorded for 8 patients in the entire cohort, 5 of them from Namibia.

Long-Term Follow-Up

LTFU was highest in the first year after diagnosis (supplemental eTable 1), and the proportion varied by registry. Namibia had the lowest fraction of patients with LTFU after diagnosis. Median follow-up time ranged from <1 year in Brazzaville, Bulawayo, and Cotonou to almost 5 years in Namibia. LTFU was not differential by age or stage at diagnosis among patients with a known stage. However, for patients without stage recorded, there was a more than 2-fold increased risk of LTFU compared with patients diagnosed at an early stage.

Survival

The overall observed survival in this cohort was 84.0% (95% CI, 80.5%–86.9%) at year 1, 58.9% (95% CI, 54.0%–63.5%) at year 3, and 47.2% (95% CI, 41.1%–53.1%) at year 5 (Figure 2). Patients with curable BC who received adequate therapy had better overall survival compared with those who received inadequate or no therapy (Figure 2). Figure 2 also shows overall survival for patients with metastatic disease, showing the poorest survival rates irrespective of the therapy received.

Table 2. Population-Based Registries Included in the Study

Registry	Country-Level HDI 2015	Period of Diagnosis	Patients With BC During Study Period n	DCO During Study Period Excluded n (%)	Population-Based Cohort n	Sampling Fraction	Traced Cohort ^b n (%)	Included for Survival Analyses n (%)
Abidjan, Cote d'Ivoire	Low	2012–2013	531	23 (4.3)	66	12.4%	50 (75.8)	53 (80.3)
Addis Ababa, Ethiopia	Low	2012	437	0 (0.0)	114	26.1%	51 (44.7)	93 (81.6)
Bamako, Mali	Low	2012–2013	639	5 (0.8)	90	14.1%	48 (53.3)	47 (52.2)
Brazzaville, Congo	Low	2012–2013	212	0 (0.0)	75	35.4%	19 (25.3)	75 (100)
Bulawayo, Zimbabwe	Low	2012–2013	167	16 (9.6)	56	33.5%	35 (62.5)	53 (94.6)
Cotonou, Benin	Low	2013–2014	132	0 (0.0)	92	69.7%	85 (92.4)	92 (100)
Eldoret, Kenya	Medium	2009–2014	379	17 (4.5)	81	21.4%	62 (76.5)	69 (85.2)
Kampala, Uganda	Low	2012–2013	283	8 (2.8)	58	20.5%	35 (60.3)	41 (70.7)
Maputo, Mozambique	Low	2014–2015	81	14 (17.8)	43	53.1%	34 (79.1)	41 (95.4)
Nairobi, Kenya	Medium	2012–2013	722	38 (5.3)	57	7.9%	37 (64.9)	55 (96.5)
Namibia	Medium	2012–2013	454	0 (0.0)	77	17.0%	61 (79.2)	64 (83.1)
Total		2009–2015	4,037	121 (3.0)	809	20.0%	517 (63.9)	684 (84.6)

Abbreviations: BC, breast cancer; DCO, death certificate–only patients; HDI, Human Development Index.

^bAdditional data on diagnostics, therapy, and/or outcome revealed after active record-finding.

Excess Mortality From Nonmetastatic BC

We assessed the excess mortality rate ratio among women with nonmetastatic disease and with at least 30 days of follow-up. Age at diagnosis was not an independent prognostic factor after adjusting for the effects of stage, tumor grade, therapy, and registry country-level HDI ($P=.389$). Being diagnosed with stage III BC compared with stages I and II BC was associated with a more than 3-fold increased risk of death rate ratio (risk ratio [RR], 3.83; 95% CI, 1.81–6.11; Figure 3). Patients who received inadequate or no therapy had more than double the risk of death compared with patients who initiated adequate therapy (Figure 3). Mortality risk did not differ by registry HDI (low vs medium).

Concerning specific therapy modalities (supplemental eFigure 5), not receiving oncologic surgery was associated with an increased risk of death compared with receiving surgery (RR, 1.67; 95% CI, 1.06–2.65). Having suboptimal chemotherapy was associated with a more than 2-fold increased risk of death (RR, 2.38; 95% CI, 1.24–4.57) compared with receiving >85% of the prescribed chemotherapy regimen. Receipt of RT was not associated with a difference in mortality risk. Nonreceipt of endocrine therapy was associated with an approximately 3-fold increased mortality risk (RR, 3.11; 95% CI, 1.50–6.10). When we

conducted sensitivity analyses, limiting the analyses just to traced patients and excluding Brazzaville (with >50% LTFU at year 1), these observed associations remained unchanged.

Discussion

Main Findings in the Context of Previous Studies

BC is a curable disease when diagnosed early and treated according to guidelines. This study shows the tenuous situation of women with BC in SSA; most patients are diagnosed at an advanced stage and only a small proportion receive guideline-concordant therapy. Of 809 women from 11 PBCRs in 10 countries, we traced 517 patient records (63.9%) and obtained detailed therapy information. Two in 3 patients (67.2%) with known stage were diagnosed with stage III or IV BC; however, given the limited access to advanced radiologic tools such as CT scans, bone scintigrams, and MRIs, this proportion may be even higher. Of traced patients with curable BC, 50.9% received inadequate or no CDT. Of all traced patients, the HRS was known for 27.5% of patients, making the use of current therapy guidelines challenging. The proportion of patients who received adequate therapy varied by registry (with patients in relatively richer countries receiving

Table 3. Cohort Characteristics

Characteristic	Population-Based Cohort n (%)	Traced Cohort n (%)
Total, N	809	517
Age at diagnosis		
20–34 y	129 (15.9)	78 (15.1)
35–49 y	300 (37.1)	196 (37.9)
50–64 y	273 (33.8)	175 (33.9)
≥65 y	107 (13.2)	68 (13.1)
Additional information found		
Yes (traced cohort)	517 (63.8)	—
No additional information except registry data	292 (36.2)	—
Hospital type		
Public hospital	405 (50.1)	385 (74.5)
Private hospital	119 (14.7)	94 (18.2)
Unknown	285 (35.2)	38 (7.3)
ECOG performance status		
0/1	144 (17.8)	144 (27.8)
2	31 (3.8)	31 (6.0)
3	19 (2.4)	19 (3.7)
4	4 (0.5)	4 (0.8)
Unknown	611 (75.5)	319 (61.7)
Tumor size		
≤5 cm (T1–T2)	120 (14.8)	110 (21.3)
>5 cm (T3–T4)	257 (31.8)	252 (48.7)
Unknown	432 (53.4)	155 (30.0)
Nodal involvement		
Present	89 (11.0)	85 (16.4)
Absent	256 (31.6)	248 (48.0)
Unknown	464 (57.4)	184 (35.6)
TNM stage		
I	12 (1.5)	10 (1.9)
II	130 (16.1)	119 (23.0)
III	201 (24.8)	191 (36.9)
IV	90 (11.1)	85 (16.4)
Unknown	376 (46.5)	112 (21.7)
Tumor grade		
1	32 (4.0)	32 (6.2)
2	124 (15.3)	124 (24.0)
3	85 (10.5)	85 (16.4)
Unknown	568 (70.2)	276 (53.4)
HRS		
ER/PR-negative	45 (5.5)	45 (8.7)
ER/PR-positive	97 (12)	97 (18.8)
Unknown	667 (82.5)	375 (72.5)

(continued)

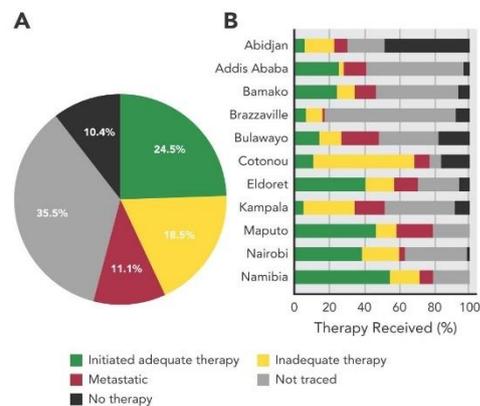
Table 3. Cohort Characteristics (cont.)

Characteristic	Population-Based Cohort n (%)	Traced Cohort n (%)
HER2 status		
Positive	43 (5.3)	43 (8.3)
Negative	87 (10.8)	87 (16.8)
Unknown	679 (83.9)	387 (74.9)
Therapy received		
Surgery	332 (41.0)	332 (64.2)
Chemotherapy	289 (35.7)	289 (55.9)
Radiotherapy	135 (16.7)	135 (26.1)
Endocrine therapy	148 (18.3)	148 (28.6)
None recorded	102 (12.6)	102 (19.7)
Unknown	292 (36.1)	—

Abbreviations: ER, estrogen receptor; HRS, hormone receptor status; PR, progesterone receptor.

more comprehensive therapy), accounting for some of the differences in survival observed across different SSA countries.

Adequate BC therapy requires a multidisciplinary approach and is resource-intensive. Many of the women in our cohort received only fragmented care or none at all. Limited access to these main forms of therapy has been described for SSA,¹² linked to both geographic and financial inaccessibility, with most women having to pay out-of-pocket for healthcare.^{13,14} In this study, surgery was the most available therapy option, with 64.2% of women in the traced cohort having a record of surgery. Still, many women never received surgery because of either

**Figure 1.** Recorded therapy received by patients (A) in the population-based cohort (n=809) and (B) by registry area.

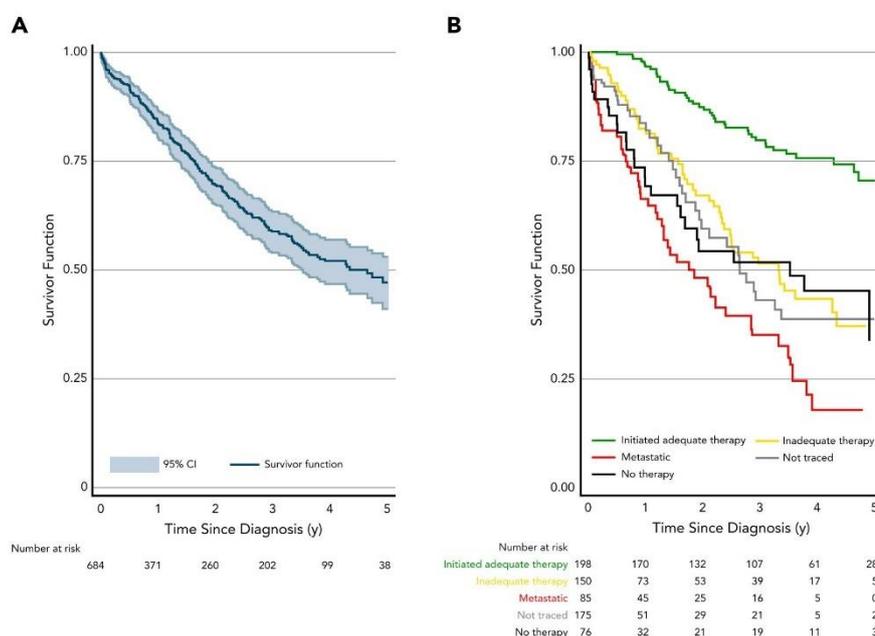


Figure 2. Overall survival (A) in the population-based cohort and (B) by therapy received.

inoperable or stage IV disease, fear of disfigurement, lack of access to surgery, or options to use neoadjuvant chemotherapy.¹⁵ Initiatives to task-share surgical BC care in primary and secondary healthcare facilities (vs tertiary healthcare facilities) have been proposed to increase the accessibility of this essential intervention.¹⁶ The main type of surgery received was mastectomy, in line with recommendations for areas with limited access to RT. However, in terms of emotional and social coping, mastectomy is often difficult for patients,¹⁷ particularly young patients in the absence of counseling and with limited access to reconstructive surgery.

Systemic treatment of BC requires specialists. In a review of the oncologic workforce worldwide, it was estimated that in 25 of the 32 African countries represented, there was approximately 1 clinical oncologist per 1,000 incident patients.¹⁸ Of the countries included in this study, this number ranged from 1 clinical oncologist per 325 incident patients in Namibia to 1 per 10,167 incident patients in Ethiopia. In the United States, there is approximately 1 clinical oncologist per 137 incident patients. Chemotherapy is not readily available; of traced patients, >40% of those with locally advanced cancer received no chemotherapy. This led to decreased survival; receiving suboptimal or no chemotherapy was associated with a poorer

prognosis compared with completing the treatment regimen. These results must be interpreted with care because reverse causation is possible (see “Limitations”).

Concerning RT, in 2010, it was estimated that in Africa there was <1 RT machine per million people, compared with almost 15 RT machines per million people in North America.¹⁹ Even within Africa, there are significant disparities in access: 60% of RT facilities are found in southern and northern Africa, with 23 countries without any RT facilities.¹⁹ The NCCN Harmonized Guidelines for SSA⁹ acknowledge this deficit in the therapy recommendations, and provide therapy guidelines that could be followed in the absence of RT facilities. Most of the patients in our cohort were candidates for RT, but only 1 in 4 traced patients received it. Of the 10 countries included, RT was available in only 5 of these countries at the time of the study: Ethiopia, Kenya, Namibia, Uganda, and Zimbabwe. A few patients from registries without in-country RT facilities had traveled abroad to receive the treatment. RT is necessary not only for curative purposes but also for palliation; approximately 70% of patients present at advanced stages with limited access to opioid analgesics in the region.^{20, 21} RT further decreases the risk of locoregional recurrence and mortality for women with stage III BC.²²

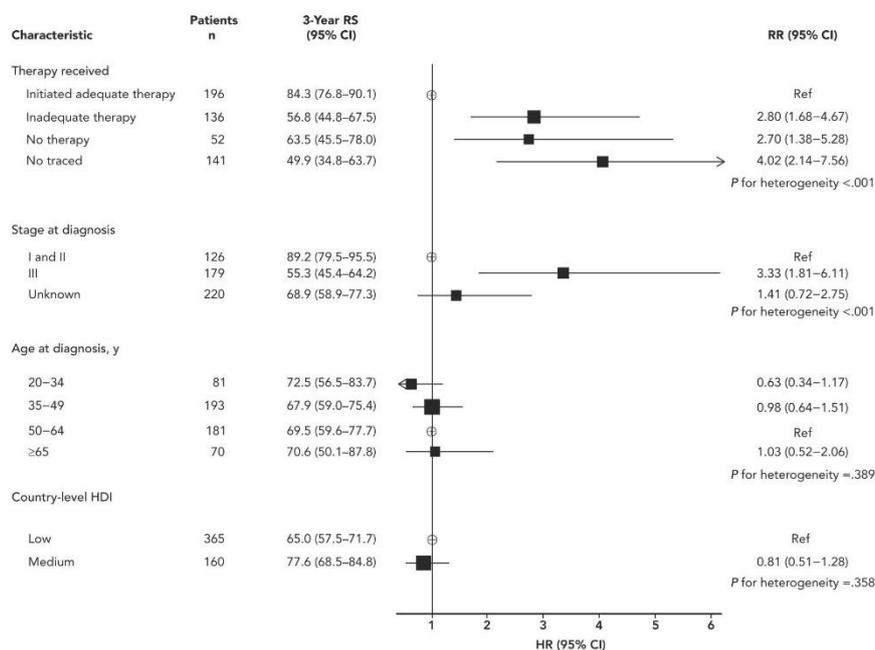


Figure 3. Three-year RS and excess risk of death from breast cancer among women in the population-based cohort without known metastases and with at least 30 days of follow-up ($n=525$) adjusted for therapy, stage, age, and country-level HDI. Abbreviations: HDI, Human Development Index; HR, hazard ratio; RR, risk ratio; RS, relative survival.

Endocrine treatment is effective for hormone receptor-positive tumors, has few adverse effects, and could be available at comparatively low costs. However, the HRS was unknown for 72.5% of the traced patients. In some of the registry areas included in this study, there was only 1 (Addis Ababa, Cotonou) or no (Bamako) laboratory with immunohistochemistry facilities for HRS testing.²³ The NCCN Harmonized Guidelines for SSA⁹ present the standard-of-care situation with the availability of HRS and do not make recommendations for treatment when the HRS is unknown. Previous recommendations have suggested giving endocrine therapy to women with locally advanced BC even with unknown HRS.²⁴ Patients who did not initiate endocrine therapy in this study had a more than 2-fold increased hazard of death compared with those who did initiate endocrine therapy, after accounting for the effect of stage and other therapy modalities.

Access to these different treatment modalities varied by registry, as seen in Figure 1. Of the registries included in our study, the Namibian national healthcare system provides free therapy for patients with cancer,⁹ including transport service to and from remote areas. This level of access seemed to be reflected in physicians actually seeing

the highest proportion of patients who initiated adequate therapy (Figure 1). Such government policies may serve as an example for best practices in access to “oncology health service for all” for patients who most likely otherwise fall out of the system. There was less comprehensive or nonexistent health coverage at public hospitals for all the other registries at the time of this study, leading to high disparities within countries. Even where government subsidies exist, medication stock-outs, indirect medical costs, and breakdowns of RT machines make completing therapy challenging,²⁵ as do the indirect costs of transport, accommodation, and supportive therapy.

A recent hospital-based study that prospectively included 2,228 patients with BC presented the survival effects of different risk factors, including the impact of late stage, lack of treatment, tumor biology, positive HIV status, and age. Notably, little education, poor awareness, rural residence, and lower socioeconomic status were associated with poorer survival outcomes. The authors showed that survival improvement (up to 22%) was achievable through downstaging and the availability of basic treatment. Patients from Namibia showed much better outcomes compared with patients from South Africa,

Uganda, Zambia, and Nigeria.²⁶ This better 3-year survival for patients from Namibia is similar to findings from the population-based registries included in the current study.⁵

Thus, although therapy guidelines are useful tools to help ensure good-quality cancer care in low- and middle-income countries, patients in resource-poor settings still face challenges such as differences in access to quality cancer diagnostics and care, especially in settings where treatment costs are not subsidized.

Limitations

A limitation of our study is its retrospective nature, which is prone to biases, and the difficulties of obtaining complete treatment data retrospectively in these settings. In addition, we could not measure and control for all potential confounders. We did not adjust for the time until onset of therapy (delay) in the final model because it was not consistently recorded for many patients. We could not measure and adjust for other factors that could influence survival, such as adherence to endocrine therapy and RT, comorbidities, molecular tumor type, and nutritional status, along with psychosocial factors influencing patient acceptance of diagnosis and therapy. In addition, relatively large proportions of patients were lost to follow-up in the first year after diagnosis, despite the active methods used to ascertain their vital status, which could result in an overestimation of survival. These high proportions of LTFU were linked to a lack of plans for patient navigation and retention and equally poor recordkeeping in some of these health systems. There could equally be the risk of immortal time bias in some of the associations seen²⁷; for instance, only women who survived long enough postsurgery could be prescribed systemic therapy. We tried to minimize this bias by excluding patients who died or were lost to follow-up within the first 30 days. A correlation between the severity of disease and choice of therapy or “confounding by indication” is a challenge in observational studies.²⁸ The relative contribution of these different therapy modalities to survival outcomes would ideally be disentangled with the use of randomized controlled trials. However, randomized controlled trials to measure outcomes in relation to the basic therapy options we investigated are not ethically feasible—thus observation and sensible deduction are the only courses available, with very careful interpretation of any observed associations between prognostic factors and outcome.

The records of 36.1% of patients registered in the PBCRs could not be traced to a treatment facility. We assumed that many of these patients never actually initiated therapy, and therefore never had a clinical treatment file opened after the pathology report. However, inadequate paper-based record systems and the absence of technological frameworks to facilitate record linkage could be a reason for the lack of tracing.

Despite these limitations, this study provides a clearer picture of the actual therapy received by a random sample of women with BC in SSA at the population level, not simply among patients attending reference treatment centers. We included women from both public and private institutions from 10 countries and patients with no record of therapy, reflecting different pathways to care, thus providing a deeper insight into the therapy routinely received by women in SSA and how this influences their survival.

Conclusions

In SSA, most women are diagnosed with BC before 50 years of age, and have a <50% chance of surviving 5 years after diagnosis. Many patients do not have access to adequate cancer therapy or—even worse—receive inappropriate cancer care with limited survival benefits and potential adverse effects. The resulting impact of lost health and productivity cannot be overemphasized. Improving access to adequate cancer therapy to prolong life, prevent recurrence, reduce stigma, and alleviate pain is necessary. Adequate therapy requires awareness of therapy options, willingness to receive conventional medical therapy, availability of these resources locally, and the means to finance healthcare. Our study sites are almost all large urban centers; access to care would even be poorer in rural settings, with more limited awareness, fewer health facilities, longer travel time to access care, and even lower ability to pay for healthcare. Despite these conditions, there are approaches available to improve access to adequate care in SSA.

Governments and nongovernmental organizations should keep working toward improving the infrastructure, such as availability of HRS testing and cancer care facilities locally based on the strategies outlined in the NCCN Harmonized Guidelines for SSA⁹ so that guideline-concordant treatments can effectively be administered. It is imperative to improve recordkeeping and data management facilities to support patient monitoring and retention and to facilitate cancer surveillance and implementation research. The inherent challenge remains financing healthcare in low-resource settings. In the meantime, we must keep emphasizing improving awareness and facilitating access to quality care to help downstage BC and improve survival outcomes. A greater focus on systemic and systematic building of infrastructure is needed to overcome the huge discrepancy between well-known effective cancer care and what is actually received on the ground.

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Chapitre II. OBJECTIFS ET CADRE

II .1. Objectifs

Les objectifs de cette thèse étaient les suivants :

II.1.1. Objectif général

Contribuer à une meilleure connaissance du fardeau et des facteurs pronostiques du cancer du sein au Bénin et en Afrique au Sud du Sahara

II.1.2. Objectifs spécifiques

- 1- Identifier les facteurs pronostiques du cancer du sein au Bénin et en Afrique au Sud du Sahara
- 2- Evaluer la capacité des Hôpitaux d’Afrique subsaharienne à prendre en charge le cancer du sein
- 3- Etudier l’incidence du cancer du sein au Bénin
- 4- Etudier la mortalité du cancer du sein au Bénin

II.2. Cadre

II.2.1. L’Afrique au Sud du Sahara

L’Afrique au Sud du Sahara est, étymologiquement, la zone du continent africain située au sud du désert du Sahara.

L’Afrique au Sud du Sahara compte 49 pays répartis en 4 sous-régions (Koduah Owusu et al., 2019)

- l’Afrique de l’Ouest (16 pays) : Bénin, Burkina Faso, Cap-Vert, Cote d’Ivoire, Gambie, Ghana, Guinée, Guinée-Bissau, Liberia, Mali, Mauritanie, Niger, Nigeria, Sénégal, Sierra Leone, Togo
- l’Afrique centrale (8 pays) : Cameroun, République Centrafricaine, Tchad, Congo, République Démocratique du Congo, Guinée Equatoriale, Gabon, Sao Tomé Principe
- l’Afrique de l’Est (15 pays) : Burundi, Djibouti, Erythrée, Ethiopie, Kenya, Rwanda, Somalie, Soudan, Soudan du Sud, Ouganda, Tanzanie, Madagascar, Comores, Maurice, Seychelles
- l’Afrique Australe (10 pays): Afrique du Sud, Angola, Botswana, Eswatini, Lesotho, Malawi, Mozambique, Namibie, Zambie, Zimbabwe

La population de l’Afrique subsaharienne était estimée à environ 1,1 milliard d’habitants en 2019. Selon la division population des Nations Unies, la population d’ASS devrait croître rapidement à un taux annuel moyen de 2,7 % pour doubler (2,2 milliards) d’ici 2050 (Falchetta et al., 2020). La **figure 6** est une carte du continent africain montrant les pays d’Afrique au Sud du Sahara et le Bénin en particulier.

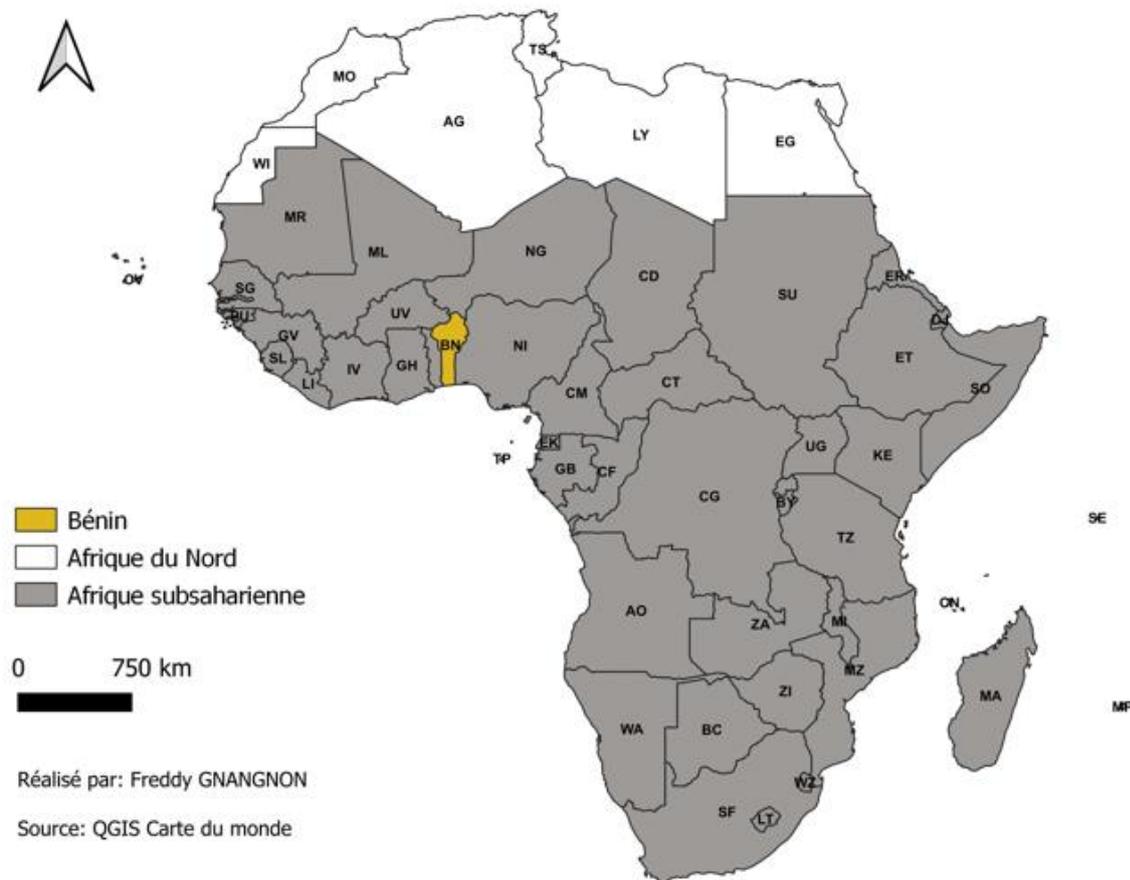


Figure 6 : Carte du continent africain montrant les pays d’Afrique au Sud du Sahara et le Bénin.

II.2.2. Les hôpitaux en Afrique Subsaharienne

Selon Falchetta et al., en Afrique subsaharienne, "au moins un sixième de la population vit à plus de deux heures d'un hôpital public, et une personne sur huit se trouve à au moins une heure du centre de santé le plus proche" (Falchetta et al., 2020). En outre, selon les estimations (Juran et al., 2018) sur une étude conduite dans 47 pays d'Afrique subsaharienne, il y aurait en moyenne 0,5 hôpital régional ou de district pour 1 000 000 d'habitants.

Cette faiblesse des infrastructures, associée à la pénurie de ressources humaines spécialisées et à l'incapacité des patients à payer le traitement du cancer du sein contribue à la mortalité relativement élevée observée en ASS (Vanderpuye et al., 2021). En outre, les établissements de soins de santé des pays d'Afrique subsaharienne sont confrontés à une pression croissante due à l'augmentation de la population et à l'émergence de maladies infectieuses (VIH, tuberculose, Ebola et COVID-19 par exemple) et de maladies non transmissibles dont le cancer (Falchetta et al., 2020).

II.2.3. Le Bénin

Le Bénin est un pays francophone de l'Afrique de l'Ouest, situé dans la zone tropicale entre l'équateur et le tropique du Cancer (entre les parallèles 6°30' et 12°30' de latitude nord et les méridiens 1° et 30°40' de longitude est) avec une superficie de 114.763 km². Il a pour capitale politique, la ville de Porto-Novo ; tandis que Cotonou est sa capitale économique. Il est limité au Nord par le Niger, au Nord-Ouest par le Burkina-Faso, au Sud par l'Océan Atlantique, à l'Est par le Nigeria et à l'Ouest par le Togo (Graeme Villeret, 2021). Le pays s'étend sur une longueur (axe nord-sud) de 700km et une largeur de 325 km sur la partie la plus large au nord. Son climat est intertropical chaud et humide avec 4 saisons au Sud et 2 grandes saisons au Nord où le climat est plutôt de type sahélien (Graeme Villeret, 2021).

Sur le plan démographique, les données du quatrième recensement général de la population et de l'habitation effectué en 2013 par l'Institut National de la Statistique et de la Démographie (INStaD) du Bénin, estimaient la population à 10.008.749 habitants dont 51,2 % de femmes, avec une densité moyenne de 87,2 habitants au km² et un taux d'accroissement naturel de 3,52 % par an (Institut National de la Statistique et de la Démographie, 2018). Cette population est estimée en 2021 à 12 506 347 habitants avec 56,9% de sujets âgés de moins de 20 ans et moins de 10% de sujets âgés de plus 50 ans (Graeme Villeret, 2021).

Le PIB par habitant du Bénin était de 1238 Euro en 2022 (country economy, 2022) avec une espérance de vie de 59,8 ans en 2021 (Countrymeters, 2023). Le Bénin est administrativement subdivisé en 12 départements, 77 communes et 546 arrondissements (Salami et al., 2017).

Le système sanitaire du Bénin est subdivisé en deux secteurs : le secteur public et le secteur privé.

Le secteur public a une structure pyramidale calquée sur le découpage territorial administratif. Il comporte trois différents niveaux :

- Le niveau central constitué par le Ministère de la Santé, ses programmes, les hôpitaux nationaux et centres hospitaliers universitaires tels que le CNHU-HKM et le CHU-MEL (Salami et al., 2017)
- Le niveau intermédiaire constitué par les directions départementales de la santé (DDS), leurs services et les centres Hospitaliers départementaux. Chaque département dispose d'un centre hospitalier départemental (CHD). Le niveau intermédiaire est chargé de la mise en œuvre de la politique sanitaire définie par le gouvernement, de la planification et de la coordination de toutes les activités des services de santé en périphérie (Salami et al., 2017)



- Le niveau opérationnel ou périphérique représenté par les zones sanitaires qui comprennent une à quatre communes. Au nombre de 34 et réparties sur toute l'étendue du territoire national, elles assurent la gestion sanitaire d'une zone administrative (Présidence de la République du Bénin, 2022). La zone sanitaire est en outre subdivisée en des aires sanitaires qui regroupent des villages ou quartiers (Salami et al., 2017). Une zone sanitaire assure la gestion sanitaire d'une zone administrative d'au moins 200 000 habitants.

Le secteur privé quant-à-lui, s'organise autour de la pyramide sanitaire en plusieurs composantes que sont : le secteur privé libéral, le secteur privé à vocation humanitaire et le secteur pharmaceutique.

II.2.3.1. Cotonou

Issu du dernier découpage administratif du Bénin (Loi N° 97-028 du 15 janvier 1999, 1999), la commune de Cotonou est située sur le cordon du littoral au croisement des 6°21 de parallèle Nord et de 2°25 Est (Cotonou Littoral Benin DB-City, 2021), entre le lac Nokoué et l'océan atlantique. D'une superficie de 79Km², elle est limitée au nord par le lac Nokoué, au sud par l'Océan Atlantique, à l'Est par la commune de Sèmè-Kpodji et à l'Ouest par la commune d'Abomey-Calavi (Ministère d'Etat chargé du Plan et du Développement, 2019).

Cotonou est une commune à statut particulier (Présidence de la République du Benin, 2023) divisé en 13 arrondissements, lesquels en 144 quartiers. Il s'agit de la seule commune du Bénin érigée en département (Présidence de la République du Benin, 2023). Elle abrite la présidence de la République, la majorité des institutions de la République, tous les ministères y compris le Ministère de la Santé. La plupart des ambassades et consulats sont implantés à Cotonou. On y retrouve également le siège de la majorité des industries et des entreprises commerciales du Bénin. Cette concentration des institutions républicaines, des représentations diplomatiques et des activités économiques, fait de Cotonou une commune à haut potentiel économique (Ministère d'Etat chargé du Plan et du Développement, 2019).

Selon les données du quatrième recensement général de la population et de l'habitation effectué en 2013 (RGPH4), la population de Cotonou était de 679 012 habitants contre 665 100 habitants en 2002, soit une augmentation de 13 912 habitants en dix ans, avec un taux d'accroissement intercensitaire de 0,18% (Ministère d'Etat chargé du Plan et du Développement, 2019). En tenant compte de ce taux d'accroissement, la population de Cotonou est estimée à 1 228 667 habitants en 2021(Wikipedia, 2023). Un cinquième Recensement général de la Population et de l'Habitat (RGPH5) est prévu au second semestre 2023.

Au plan sanitaire, Cotonou abrite la plupart des hôpitaux publiques du niveau central dont le Centre Hospitalier et Universitaire de Pneumo-Phtisiologie 'Lazaret', le Centre Hospitalier Universitaire

Psychiatrique “Jacquot”, le Centre National Hospitalier Universitaire Hubert Koutoukou Maga (CNHU-HKM), et le Centre Hospitalier Universitaire de la Mère et de l’Enfant Lagune (CHU-MEL). Ces deux derniers disposent de services prenant en charge les cancers. Ils constituent, à l’échelle nationale, les centres de référence pour la prise en charge du cancer du sein. La **figure 7** est une carte montrant le découpage administratif du Bénin.

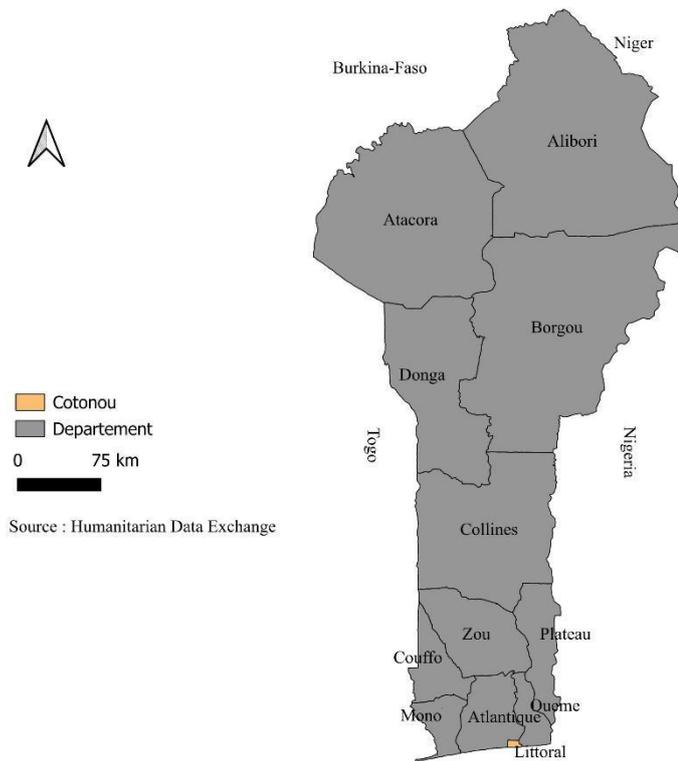


Figure 7: Carte montrant le découpage administratif du Bénin

III.1. Revue Systématique des facteurs pronostiques du cancer du sein en ASS

Le cancer du sein est un défi majeur de santé publique en Afrique au Sud du Sahara (ASS), caractérisé par des taux de mortalité élevés malgré des taux d'incidence plus faibles que ceux observés dans les pays occidentaux. Le diagnostic à un stade avancé, l'accès limité aux ressources de santé, et les disparités socioéconomiques intensifient les problèmes de gestion du cancer du sein en ASS, aggravés par les croyances culturelles et l'insuffisance des infrastructures de santé. Reconnaisant la nécessité d'interventions fondées sur des preuves, cette revue systématique vise à combler les lacunes dans les données sur les facteurs pronostiques du cancer du sein en se concentrant sur l'âge au diagnostic, le stade du cancer, le sous-type moléculaire et les résultats de survie en ASS. En synthétisant les données de 85 études impliquant 33 053 patientes, nous avons trouvé que l'âge moyen au diagnostic était de 48,7 ans, avec le stade III représentant 50%, suivi des stades II, IV et I. La distribution des sous-types moléculaires a révélé que le sous-type luminal A était le plus courant (30%), suivi du triple négatif (29%), du sous-type luminal B (18%) et du sous-type HER2+ (11%). Des variations sous-régionales ont été observées, l'Afrique du Sud affichant des profils différents de celui des autres régions. La survie à 5 ans était de 44%, avec des disparités observées entre les sous-régions, indiquant un pronostic plus sombre en Afrique de l'Ouest par rapport à l'Afrique de l'Est. Nos résultats soulignent l'urgence de mettre en œuvre des interventions ciblées pour améliorer les résultats de la prise en charge diagnostique et thérapeutique du cancer du sein en ASS, en insistant sur l'importance de la détection précoce, de l'accès à un traitement multimodal. En somme cette méta-analyse fournit des informations précieuses sur le profil pronostique du cancer du sein en Afrique subsaharienne et permet de visualiser des stratégies fondées sur des preuves afin de réduire le fardeau croissant sur les individus, les systèmes de santé et les communautés de la région.

Soumis à “The breast”: IF 5,7

The Breast
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Abstract:	Background: Breast cancer is a significant public health challenge in Sub-Saharan Africa (SSA), characterized by high mortality rates despite historically lower incidence rates compared to Western countries. Limited access to healthcare resources, late-stage diagnosis, and socioeconomic disparities intensifies the problems of breast cancer management in SSA, compounded by cultural beliefs and healthcare infrastructure deficiencies. Methods and Findings: Recognizing the need for evidence-based interventions, this meta-analysis aims to address gaps in breast cancer data by focusing on age at diagnosis, cancer stage, molecular subtype, and survival outcomes in SSA. By synthesizing data from 85 studies involving 33,053 patients, we found the average age at diagnosis to be 48.7 years, with stage III being the most prevalent at 50%, followed by stages II, IV, and I. The distribution of molecular subtypes revealed luminal A as the most common subtype (30%), followed by triple-negative (29%), luminal B (18%), and HER2+ (11%). Subregional variations were observed, with South Africa displaying distinct patterns compared to other regions. The 5-year survival rate was 44%, with disparities observed between subregions, indicating a poorer prognosis in West Africa compared to East Africa. Our findings underline the urgent need for targeted interventions to improve breast cancer outcomes in SSA, emphasizing the importance of early detection, access to comprehensive treatment facilities, and addressing regional disparities. Conclusions: This meta-analysis provides valuable information on the epidemiological profile of breast cancer in Sub-Saharan Africa. It enables evidence-based strategies to be developed for the prevention, early detection and treatment of the disease, in order to reduce the growing burden on the region's healthcare systems and communities.

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TITLE

Prognostic factors of breast cancer and survival in Sub-Saharan Africa: a systematic review and meta-analysis

SHORT TITLE

Breast Cancer Characteristics in Sub-Saharan Africa: A Meta-Analysis

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ABSTRACT

Background: Breast cancer is a significant public health challenge in Sub-Saharan Africa (SSA), characterized by high mortality rates despite historically lower incidence rates compared to Western countries. Limited access to healthcare resources, late-stage diagnosis, and socioeconomic disparities intensifies the problems of breast cancer management in SSA, compounded by cultural beliefs and healthcare infrastructure deficiencies. **Methods and Findings:** Recognizing the need for evidence-based interventions, this meta-analysis aims to address gaps in breast cancer data by focusing on age at diagnosis, cancer stage, molecular subtype, and survival outcomes in SSA. By synthesizing data from 85 studies involving 33,053 patients, we found the average age at diagnosis to be 48.7 years, with stage III being the most prevalent at 50%, followed by stages II, IV, and I. The distribution of molecular subtypes revealed luminal A as the most common subtype (30%), followed by triple-negative (29%), luminal B (18%), and HER2+ (11%). Subregional variations were observed, with South Africa displaying distinct patterns compared to other regions. The 5-year survival rate was 44%, with disparities observed between subregions, indicating a poorer prognosis in West Africa compared to East Africa. Our findings underline the urgent need for targeted interventions to improve breast cancer outcomes in SSA, emphasizing the importance of early detection, access to comprehensive treatment facilities, and addressing regional disparities. **Conclusions:** This meta-analysis provides valuable information on the epidemiological profile of breast cancer in Sub-Saharan Africa. It enables evidence-based strategies to be developed for the prevention, early detection and treatment of the disease, in order to reduce the growing burden on the region's healthcare systems and communities.

KEYWORDS

Breast cancer, Sub-Saharan Africa, Epidemiology, Meta-analysis, Survival

INTRODUCTION

Breast cancer remains a significant public health challenge worldwide, and its impact is particularly pronounced in Sub-Saharan Africa (SSA). While breast cancer incidence rates are historically lower in SSA compared to Western countries, mortality rates are disproportionately higher due to late-stage diagnosis, limited access to healthcare resources, and socioeconomic disparities (1–3). The complex

aspects of breast cancer management in sub-Saharan Africa are exacerbated by factors such as cultural beliefs, lack of screening programs, and healthcare infrastructure deficiencies (4).

Epidemiological data reveal a rising trend in breast cancer incidence across SSA, with an estimated 200,000 new cases diagnosed annually (5). Despite the increasing burden, the region faces several challenges in effectively fighting breast cancer, particularly limited access to early detection services, a lack of comprehensive treatment facilities and a need for oncology staff. These challenges contribute to delayed diagnosis and poor prognosis, resulting in a higher proportion of advanced-stage breast cancer cases at medical consultation and lower survival rates compared to high-income countries (6).

Breast cancer is a multifaceted disease with distinct molecular subtypes that significantly influence prognosis and treatment strategies. Luminal A (estrogen and progesterone receptor positive) is known for its favorable prognosis and responsiveness to hormone therapy, whereas Luminal B shows higher proliferation rates, indicative of a poorer prognosis (7). HER2-enriched subtype, characterized by overexpression of the HER2 protein, is more aggressive but amenable to targeted therapies such as trastuzumab. In contrast, Triple Negative Breast Cancer (TNBC), which lacks the three typical receptors, is the most aggressive with fewer treatment options.

The staging of breast cancer, which ranges from stage 1 to stage 4, is crucial as it not only correlates with survival rates but also informs treatment decisions. Stage 1 cancers are localized and have the highest survival rates, typically over 90%. Stage 2 and stage 3 cancers involve larger tumor sizes and/or have spread to nearby lymph nodes but are still primarily contained within the breast area, with progressively lower survival rates (8). Stage 4 breast cancer, or metastatic cancer, has spread beyond the breast and nearby lymph nodes to other parts of the body, such as bones, liver, or lungs, significantly complicating treatment and reducing survival rates (9). Understanding these stages helps clinicians tailor treatments more effectively and allows patients to make informed decisions about their care options. Moreover, studying prognostic factors like age is crucial because it affects the biological behavior of breast cancer. Younger women tend to have more aggressive cancers and may not respond as well to treatments typically effective in older patients. This understanding underscores the importance of personalized treatment plans based on individual prognostic factors to optimize outcomes for each patient.

Systematic reviews and meta-analyses play a crucial role in synthesizing existing evidence, identifying gaps in knowledge, and informing public health strategies (1,10). The present meta-analysis seeks to address the paucity of comprehensive data on breast cancer in SSA by focusing on four key parameters: age at diagnosis, cancer stage at diagnosis, molecular subtype, and survival outcomes. These parameters are essential for understanding the epidemiological profile of breast cancer in SSA and identifying areas for targeted intervention. Additionally, this meta-analysis aims to explore regional variations in disease characteristics and outcomes through cluster analysis, providing insights into the heterogeneity of breast cancer burden across different sub-regions of SSA. Our meta-analysis extends the scope of previous studies by taking these four key factors into account. While prior research focused on individual aspects, like the study of Jedy-Agba et al. on the diagnostic stage without regional distribution (11), our work comprehensively addresses these gaps. Two other studies during our timeframe focused solely on molecular subtypes, but included studies of the entire Africa including the Maghreb (12,13). The originality of our study lies in the fact that it focuses exclusively on sub-Saharan African countries, excluding the Maghreb region, and its comprehensive examination of age, stage, molecular subtype, and survival outcomes. By synthesizing data from diverse sources and employing robust statistical methods, we aim to provide a nuanced understanding of breast cancer epidemiology in SSA and inform evidence-based strategies for disease prevention, early detection, and treatment.

METHODS

Data Sources and Literature Search

This systematic review was conducted according to our protocol, which was registered in the International Prospective Register of Systematic Reviews, PROSPERO (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022310699). The study adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (25). We searched the OvidSP databases (Embase + MEDLINE + Global Health), Scopus, Web of Science, African Journals Online (using only the keywords "breast cancer"), and Google Scholar (first 210 results) for studies published in English or French between January 01, 1991, and January 01, 2022. To initiate the search, general keywords were first designed around the following basic concepts (**Table S1**). This equation includes Medical Subject Headings (MeSH) terms and was generated from the PubMed Advanced Search Builder.

Study Selection

The search equation was used across multiple search engines to compile a list of publications. Abstracts from these publications were imported into the article selection tool, Rayyan, and evaluated by two blinded readers - Alexis PARENTE (A.P.) and David KINSOU (D.K.). Duplicate articles were identified and removed using Rayyan. Subsequently, the selection process involved reviewing the title and abstract of each article against predefined inclusion and exclusion criteria agreed upon by investigators. After categorizing publications based on title and abstract, included studies underwent independent full-text assessment by investigators, mirroring the initial stage's methodology. In instances of disagreement among readers, consensus was reached.

Inclusion and Exclusion Criteria

Studies were required to be in English and/or French and had to satisfy three primary inclusion criteria outlined in the title or abstract: relevance to breast cancer, involvement of a female population, and execution within Sub-Saharan Africa. Exclusion criteria for the initial phase of title and abstract screening comprised failure to meet the inclusion criteria, absence of an available abstract, and the presence of systematic reviews or conference materials. During the subsequent phase (full-text assessment), inclusion criteria comprised breast cancer diagnoses in women aged 15 years and older within Sub-Saharan African nations, reporting on 5-year survival and/or stage distribution at diagnosis and/or age at diagnosis and/or molecular subtype distribution (including luminal A, luminal B, HER2+, and Triple negative). Additionally, qualifying study types encompassed general population, cohort, or hospital-based studies, articles published between 1991 and 2022, and studies comprising at least 30 cases of breast cancer. Exclusion criteria involved data aggregated from multiple African countries, conference abstracts, studies involving non-human subjects, those concentrating on specific age groups or characteristics, and those exclusively involving male patients.

Data Extraction

Data were extracted using a data extraction grid in Excel software, developed based on Cochrane and PRISMA-P guidelines. We were able to formalize the following analysis points: title, author, year of publication, country of study, the main objective of the study, study type, size of the study population, type of population studied, variables of interest (mean age at diagnosis with standard deviation and extremes if available; the proportion of patients presenting with stages I, II, III, and IV at diagnosis, or early (I/II) and late (III/IV) stages if only this combined information was provided; the proportion of patients with Luminal A, Luminal B, HER2+, and triple negative breast cancer at diagnosis; 5-year survival after diagnosis) as well as the sample size from which each of these variables were extracted if different from the study population size. The timing of diagnosis in the original articles corresponds to the clinical or pathological diagnosis moment. If there were multiple articles covering the same study period, context, and author, the article containing the most information on the variables of interest for our review was selected.

Quality Assessment of Studies

Two independent reviewers assessed the quality of the included articles using the STROBE criteria (Strengthening the Reporting of Observational Studies in Epidemiology). This checklist, comprising 22 items, evaluates various aspects of study reporting, including participant selection, eligibility criteria, follow-up procedures, handling missing data, outcome measurement, and study size. Scores, presented as a percentage of fulfilled criteria out of the total, allowed for comparison across studies. A detailed STROBE checklist and explanation document guided the assessment process, ensuring consistency and comprehensiveness.

Data Analysis

For age at diagnosis, the statistic of interest was the mean age and its standard deviation. For stage, molecular subtype, and survival, the statistic of interest was the proportion of breast cancers diagnosed at different stages and for each subtype as well as the survival after a five-year follow-up. Meta-analyses were conducted using R software version 4.2.0, utilizing the `metaprop` and `metamean`. The results of the meta-analysis on pooled mean data and various proportions are presented below, by using random effects to explore heterogeneity among studies further. We calculated I² statistics and used forest plots visualizing study-specific estimates and the pooled random effect estimators. Publication bias was assessed using Begg's funnel plot and Egger's test and was found to be high ($P < 0.001$). Heterogeneity due to continent was evaluated via meta-regression and was found to be not significant.

RESULTS

Characteristics of Included Studies

The initial search in OvidSP (Embase + MEDLINE + Global Health), Web of Science, African Journals Online, and Google Scholar yielded 7210 abstracts. After eliminating duplicates, we retained 4134 publications, which were analyzed through a selection process based on titles and abstracts. We identified 176 articles as potentially relevant, and their full texts were examined. Ultimately, we selected 94 studies that met the inclusion criteria (14–107) (**Figure 1**). These 94 studies involved 33053 patients, with sample sizes ranging from 32 to 2154. Most studies had a sample size of over 100 patients with known information. Only seven studies included more than 1000 women diagnosed with breast cancer (14,26,35,37,40,41,47). The oldest study included was conducted in 1991 (14), and the most recent was in 2022 (107). Most studies were carried out in Nigeria and South Africa, with 20 and 13 studies, respectively, followed by Ethiopia, Kenya, and Tanzania, each with 9 studies. The detailed baseline characteristics of the studies included in this meta-analysis are described in **Table S2**.

The median score for study quality was 15.5/22 (70%). Based on this evaluation, 85 out of 94 studies were deemed of intermediate to high quality, while 9 out of 94 were classified as low quality (16,32,44,49,51,53,57,68,70). Details of the assessment and the scores obtained for each article are presented in **Table S3**. We excluded these 9 articles, leaving us with 85 included studies. However, three studies involved two distinct and independent populations, thus each counted as two separate studies, resulting in a total of 88 studies truly incorporated into our meta-analysis. Among these studies, 45 provided information on age, 55 on stage at diagnosis, 38 on molecular subtype, and 14 on 5-year survival. Several articles provided information on at least 2 of our variables of interest.

Age and stage at breast cancer diagnosis in SSA

The average age at breast cancer diagnosis among included patients was 48.7 years in SSA [47.7; 49.7] (**Figure 2**). This varies depending on the studied subregion, reaching a maximum of 55.4 years [54.8; 56.0] in South Africa and a minimum of 48.0 [47.0; 49.1] in West Africa.

The results of the analysis revealed the following frequencies of cancer stages in SSA, with Stage III being the most prevalent, followed by Stage II, Stage IV, and finally Stage I. Stage III cancer had a combined frequency of 0.50 (95% CI, 0.46 to 0.54; I² = 91%) (**Figure 3**). When examining by region, Central Africa demonstrated the highest frequency at 0.55 (95% CI, 0.38 to 0.71; I² = 98%), while South Africa displayed the lowest at 0.44 (95% CI, 0.35 to 0.54; I² = 72). Stage I cancer had a combined

frequency of 0.04 (95% CI, 0.03 to 0.05; I2 = 89%) (**Figure S1**). Its prevalence was lowest in West Africa at 0.03 (95% CI, 0.01 to 0.19; I2 = 72), and higher in South Africa at 0.06 (95% CI, 0.03 to 0.11; I2 = 94%). Stage II cancer exhibited a pooled frequency of 0.22 (95% CI, 0.18 to 0.26; I2 = 96%) (**Figure S2**). South Africa showed the highest frequency within regions at 0.25 (95% CI, 0.17 to 0.35; I2 = 91%), whereas West Africa had the lowest at 0.19 (95% CI, 0.13 to 0.25; I2 = 94%). Lastly, Stage IV cancer presented a combined frequency of 0.12 (95% CI, 0.08 to 0.18; I2 = 96%) (**Figure S3**). West Africa had the highest frequency regionally at 0.21 (95% CI, 0.11 to 0.37; I2 = 94%), while South Africa displayed the lowest at 0.06 (95% CI, 0.03 to 0.15; I2 = 97%).

Distribution of molecular subtypes of breast cancer in ASS

After analyzing the results, the frequencies of breast cancer subtypes in SSA were observed in the following order: luminal A, triple-negative, luminal B, and HER2+. The combined frequency of the luminal A subtype in SSA was 0.30 (95% CI, 0.25 to 0.36; I2 = 95%) (**Figure S4**). Its prevalence was lowest in South Africa at 0.27 (95% CI, 0.16 to 0.43; I2 = 99%) and slightly higher in East Africa/West Africa at 0.31 each. Next, the pooled frequency of triple-negative breast cancer (TNBC) subtype in SSA was 0.29 (95% CI, 0.25 to 0.33; I2 = 95%) (**Figure 4**). West Africa exhibited the highest frequency regionally at 0.37 (95% CI, 0.31 to 0.44; I2 = 94%), while South Africa showed the lowest at 0.17 (95% CI, 0.12 to 0.24; I2 = 81%). The pooled frequency of the luminal B subtype in SSA was 0.18 (95% CI, 0.13 to 0.24; I2 = 97%) (**Figure S5**). South Africa displayed the highest frequency regionally at 0.41 (95% CI, 0.23 to 0.62; I2 = 99%), while West Africa had the lowest at 0.11 (95% CI, 0.06 to 0.17; I2 = 90%). Lastly, the combined frequency of the HER2+ subtype in SSA was also 0.11 (95% CI, 0.09 to 0.13; I2 = 79%) (**Figure S6**). East Africa/West Africa showed the highest frequency at 0.12 each, while South Africa displayed the lowest at 0.09 (95% CI, 0.06 to 0.14; I2 = 66%).

Analysis of 5-year survival in breast cancer in SSA

Our meta-analysis demonstrates that the 5-year survival rate of breast cancer in SSA is 0.44 (95% CI, 0.32 to 0.57; I2 = 96%) (**Figure 5**). The 5-year survival rate is poorer in West Africa with a frequency of 0.34 (95% CI, 0.17 to 0.56; I2 = 98%), while it is better in East Africa with a survival rate of 0.48 (95% CI, 0.35 to 0.62; I2 = 95%).

DISCUSSION

Breast cancer remains a major challenge for global health, with Sub-Saharan Africa suffering particularly severe effects. In SSA, factors such as late-stage diagnoses, restricted access to healthcare resources, and marked socioeconomic disparities lead to mortality rates that are notably higher than those in Western countries (2). Our meta-analysis was designed to investigate the epidemiological characteristics of breast cancer in SSA, specifically targeting age at diagnosis, cancer stage, molecular subtype, and survival outcomes. The special feature of our study is that it focuses on sub-Saharan Africa, explicitly excluding the Maghreb region. We conducted an in-depth analysis of age, cancer staging, molecular subtypes and survival rates. By integrating data from a variety of sources and using rigorous statistical techniques, our goal was to enhance the understanding of breast cancer epidemiology in SSA and support the development of evidence-based interventions for disease prevention, early detection, and treatment. Our findings address significant gaps in existing literature by providing a holistic view of breast cancer epidemiology in SSA, unlike previous studies which tended to isolate specific aspects such as diagnostic stages or molecular subtypes without a broader epidemiological context (11). This comprehensive approach allowed us to systematically assess and compare age, stage, molecular subtype, and survival outcomes throughout SSA, offering critical insights for improving healthcare strategies in the region.

Our meta-analysis revealed a relatively young age for breast cancer diagnosis in Sub-Saharan Africa (SSA), averaging 48.7 years, with regional variations. This early onset underlines the need for appropriate action and age-adapted screening programs to facilitate timely diagnosis and improve

outcomes (108). Comparisons with high-income regions highlight differences in age distribution, emphasizing the interplay of genetic, environmental, and socioeconomic factors influencing breast cancer epidemiology. , To overcome the early age of diagnosis, multi-faceted approaches are needed, encompassing education, primary prevention and improved access to screening and diagnostic services, with the aim of ultimately contributing to improved breast cancer outcomes in Sub-Saharan Africa. (109).

A significant outcome of our meta-analysis is the over-representation of the triple-negative breast cancer subtype (TNBC) in Sub-Saharan Africa, which stands in contrast to trends observed in Europe and other high-income regions. In SSA, TNBC accounted for a pooled frequency of 29%, significantly higher than rates reported in Europe and North America. This overrepresentation of TNBC in SSA has been attributed to various factors, including genetic predisposition, environmental exposures, and limited access to screening and early detection services. Studies have shown that TNBC is more prevalent among younger women and those of African ancestry, suggesting a potential genetic component contributing to its higher frequency in SSA populations (110). The implications of the overrepresentation of TNBC in SSA are profound, as TNBC is associated with poorer survival outcomes compared to other breast cancer subtypes (111).

There are many reasons for late diagnosis in sub-Saharan Africa, and among them are difficulties in the healthcare system, particularly limited access to screening programs, inadequate diagnostic resources and socio-economic disparities (112). Studies have shown that a significant proportion of breast cancer cases in SSA are diagnosed at advanced stages, with stage II being overrepresented compared to stage I (113). Efforts to address the overrepresentation of TNBC in SSA must prioritize improving access to early detection services, promoting breast cancer awareness, and enhancing healthcare infrastructure. Implementing population-wide screening programs, sensitizing healthcare professionals and the public to the importance of early detection, and strengthening diagnostic and treatment infrastructures are crucial steps towards reducing diagnosis times and improving outcomes for breast cancer patients in sub-Saharan Africa.

Our meta-analysis provides valuable insights into the 5-year survival rates of breast cancer patients in Sub-Saharan Africa (SSA). The findings underscore significant disparities in survival outcomes across different regions within SSA, highlighting the complex interplay of socioeconomic, healthcare access, and disease-related factors that influence breast cancer prognosis in the region.

Our meta-analysis highlights significant disparities in the 5-year survival rates of breast cancer patients across Sub-Saharan Africa, with an overall rate of 44%. Regional variations revealed lower survival rates in West Africa (34%) compared to East Africa (48%), reflecting differences in healthcare infrastructure, access to quality care, and disease awareness. Comparisons with survival rates reported in high-income countries demonstrate the substantial gap in breast cancer outcomes between SSA and more developed regions. For instance, studies conducted in Europe and North America have reported 5-year survival rates exceeding 80% for breast cancer patients, indicating significantly better prognosis and treatment outcomes compared to SSA. This disparity in survival rates clearly and urgently requires targeted interventions to improve cancer management, strengthen healthcare systems, and overcome socioeconomic barriers to access to care in SSA.

However, our study has certain limits that need to be addressed. Despite our efforts to include as many relevant studies as possible, the quality of the included studies was inconsistent, and some studies were excluded due to low quality or insufficient data. Additionally, while our meta-analysis provides valuable insights into breast cancer epidemiology in SSA, further researches are needed to explore additional factors influencing breast cancer outcomes, such as access to healthcare services, cultural beliefs, and socioeconomic factors (114).

In conclusion, our meta-analysis provides a comprehensive overview of breast cancer epidemiology in SSA, highlighting the urgent need for evidence-based interventions and policy decisions to improve outcomes in the region. By addressing critical gaps in knowledge and providing valuable insights into age at diagnosis, cancer stage, molecular subtype distribution, and survival outcomes, our study contributes to the growing literature on breast cancer in SSA and informs targeted strategies for disease prevention, early detection, and treatment.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

AUTHORS' CONTRIBUTIONS

AP, FHRG and VB conceived the idea for the study. FHRG, AP, DK designed the research and performed systematic review. AP, DK, CA performed statistical analyses. AP and VB wrote the paper. MC, HRS, MI, EN, TPD, DH and PMP contributed to the interpretation and writing. All authors reviewed the manuscript.

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FIGURE LEGENDS AND TABLES

Figure 1: PRISMA Flowchart of Included Studies. PRISMA flowchart detailing the selection and inclusion of studies in the meta-analysis. PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Figure 2: Pooled Average Age at Breast Cancer Diagnosis by Region. Pooled average age at diagnosis of breast cancer, stratified by different regions.

Figure 3: Regional Stratification of Stage III Breast Cancer Frequency. Pooled frequency of Stage III breast cancer cases, stratified by different regions.

Figure 4: Regional Stratification of Triple-Negative Breast Cancer Frequency. Pooled frequency of triple-negative breast cancer cases, stratified by different regions.

Figure 5: Regional Stratification of Five-Year Survival Rates. Pooled five-year survival rates for breast cancer, stratified by different regions.

III.2. Evaluation de la capacité des hôpitaux d'ASS à assurer la continuité des soins pour les patients atteints du cancer du sein

Le cancer du sein est un problème majeur de santé publique à l'échelle mondiale. La situation semble encore plus préoccupante en Afrique subsaharienne. Bien que l'incidence y soit parmi les plus faibles au monde, la mortalité y est la plus élevée ce qui témoigne d'un taux de survie particulièrement faible. La capacité du système de santé a été incriminée dans certaines études mais seules quelques-unes ont examiné les capacités des hôpitaux à fournir un continuum de soins pour le cancer du sein en Afrique subsaharienne.

Le but de ce travail était d'évaluer la disponibilité des équipements de diagnostic et des traitements adjuvants dans les hôpitaux pratiquant la chirurgie du cancer du sein en Afrique subsaharienne. Nous avons effectué une analyse secondaire des données de l'étude GlobalSurg3 (voir **annexe 1**), collectées en Afrique au Sud du Sahara.

Au total, 47 hôpitaux de 15 pays d'Afrique subsaharienne et 43 villes ont été inclus entre le 1er avril 2018 et le 31 janvier 2019. Un tiers des hôpitaux couvrait une population supérieure à deux millions d'habitants (n=17 ; 36,2%). L'échographie était disponible dans tous les hôpitaux. La moitié seulement des hôpitaux participants (n=26, 55,3%) avaient accès à un pathologiste à temps plein, tandis que les Réunions de Concertation Pluridisciplinaires (RCP) n'étaient pas disponibles dans 42,4% des hôpitaux. L'équipement pour la radiothérapie n'était disponible que dans neuf hôpitaux (19,1 %). Seule la moitié des hôpitaux (n=25, 53,1%) disposaient de médicaments de chimiothérapie. Dans neuf hôpitaux (19,1%), les patients devaient parcourir plus de 50 kilomètres pour avoir accès aux médicaments de chimiothérapie.

Il en résulte que, le pronostic des patientes atteintes d'un cancer du sein en Afrique au Sud du Sahara ne peut être amélioré sans investissements significatifs afin de fournir un diagnostic rapide et un traitement efficace.

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Assessing the continuum of care in sub-Saharan African hospitals performing surgery for breast cancer

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Abstract

While breast cancer incidence rates in SSA are among the lowest worldwide, mortality rates remain among the highest, reflecting particularly poor survival. Only a few studies in SSA have investigated the capabilities of treatment services to adequately provide a continuum of care for breast cancer. Our aim was to assess the availability of diagnostic facilities and adjuvant therapies in hospitals performing breast cancer surgery in SSA. We performed a secondary analysis of GlobalSurg3 study data collected in the SSA region. A total of 47 hospitals from 15 SSA countries and 43 cities were included between April 1, 2018, and Jan 31, 2019.

One-third of hospitals covered a population greater than two million (n=17; 36.2%). Ultrasound was available in all hospitals; however, it was not consistently functional in 11 hospitals (23.4%). Only half of the participating hospitals (n=26, 55.3%) had access to a full-time pathologist, while the multidisciplinary team (MDT) approach was not found in 42.4% of hospitals. Equipment for radiotherapy was only available in nine hospitals (19.1%). Only half of the hospitals (n=25, 53.1%) had chemotherapy drugs available on site. In nine hospitals (19.1%), patients had to travel more than 50 kilometers to access chemotherapy drugs. In conclusion, the outcome of breast cancer patients in SSA cannot be improved without significant investments in pathology, surgical and oncological treatment pathways to provide timely diagnostic and effective treatment.

NOVELTY AND IMPACT

To date, most studies aimed at assessing the management of breast cancer in Sub-Saharan Africa (SSA) use simulated methods due to the absence of robust data. Empirical and observational data on the management of breast cancer in the region are lacking. In this study, we provided country-specific information on diagnostic facilities and adjuvant therapies for breast cancer patients in SSA. We also demonstrate how addressing these inequities is essential to meet the gender equality Sustainable Development Goals of the United Nations.

INTRODUCTION

Cancer burden is rising in sub-Saharan Africa (SSA) [1], with breast cancer being the leading cause of cancer morbidity in the region [2]. In spite of this, breast cancer incidence rates in SSA are among the lowest in the world, but mortality rates remain among the highest, reflecting the particularly poor survival of breast cancer patients [2, 3].

The management of breast cancer is multidisciplinary and resource intensive. While the diagnosis is primarily based on imaging and pathology, the main pillars of treatment depend on the disease stage and include surgery, radiotherapy, and systemic therapies (chemotherapy, endocrine therapy, targeted therapies and more recently immunotherapy). In SSA, accurate disease classification and staging is usually difficult to achieve due to the lack of appropriate diagnostic tools, and the choice of a treatment

plan is often based on the availability of treatment services, with surgery representing the most popular option [8]. On the other hand, with locally advanced or metastatic disease being more frequent at the time of diagnosis [5], systemic therapies, along with radiotherapy, have become essential for treatment and palliation

While several studies have reported the advanced stage of breast cancer at the time of diagnosis in SSA, there are limited data on breast cancer diagnostic and treatment facilities and access to care in the region [4]. Although many reports highlight the need for early detection and downstaging to improve breast cancer patient survival [2, 5, 6], only a few studies have investigated the current capabilities of diagnostic and treatment services to provide quality care to patients in SSA [7].

We carried out this study to assess the availability of diagnostic, surgical and other treatment services in hospitals performing breast cancer surgery in SSA.

MATERIALS AND METHODS

Study design and study period

This study is a secondary analysis of data collected as part of the GlobalSurg 3 study, a multicenter, international, prospective, observational study of all consecutive patients undergoing surgery in hospitals providing surgical services for cancer patients (including breast cancer) around the world [8]. The GlobalSurg 3 study was conducted between April 2018 and January 2019 with validation of data performed until April 23, 2019, and the survey was developed based on a validated model that has been used successfully in previous studies [8–13]. The survey design followed a system-based approach adapting the framework for Comprehensive Cancer Centers in LMICs [14]. Beta testing at two LMIC hospital sites was performed to ensure survey clarity prior to formal release to the collaborating hospitals. For this study, we selected GlobalSurg3 data collected in SSA reporting on the availability of breast cancer diagnostic and treatment services.

Inclusion criteria

Any hospital providing emergency or elective surgery for breast cancer in SSA was eligible. We used the World Bank criteria [15] to define income groups and categorize the included countries.

Investigators

Data were collected by selected in-country investigators who were responsible for accurate uploading of data via a secure internet-based Research Electronic Data Capture (REDCap) system. Collaborators were provided with a data extraction sheet to aid completion, with reminders being sent every four weeks if the survey remained incomplete.

Data points

Hospital infrastructure and process resources identified as core clinical service components to ensure access to quality breast cancer care were captured, such as hospital coverage, the presence of imaging modalities, oncology services, surgical treatment and perioperative care [8]. We finally selected nine (09) criteria to define a hospital that can optimally provide a continuum of care for breast cancer patients undergoing surgery. These criteria were divided into four diagnostic criteria (ultrasound availability, CT scan availability, pathology services availability, waiting time for pathology report in weeks) and five therapeutic criteria (MDT availability, radiotherapy availability, type of radiotherapy, availability of chemotherapy, availability of postoperative care area).

Data analysis

Descriptive statistics were calculated with R Statistics for Windows, Version 3.5.0. Qualitative variables are presented as proportions, and quantitative variables are presented as the mean \pm standard deviation.

RESULTS

Baseline characteristics of the included hospitals

A total of 47 hospitals from 15 countries and 43 cities were included during the data collection period. Of the 15 SSA countries included in the Globalsurg 3 study, six were from Southern Africa, four from West Africa and four from East Africa. Only one country from Central Africa was included (Fig. 1A). In addition, half of the included countries (n = 8) were low-income countries according to the World Bank's classification, 2019 (Fig. 1B), and the remaining seven countries were classified as middle-income countries.

Among the included hospitals, 17 (36.2%) covered a population greater than two million, with most of the hospitals (n = 31, 65.9%) covering a population above 500 000. Most hospitals (n = 42, 86.4%) were referral hospitals located in large cities. Table 1 describes the baseline characteristics of the included hospitals.

Diagnostic Imaging and pathology services

Ultrasound was available in all hospitals; however, it was not routinely available and/or functioning in one-quarter of hospitals (n = 11).

CT scans were available in most hospitals (n = 33, 70.2%) but were nonfunctional in 12 hospitals (25.5%).

Approximately half of the hospitals (n = 26, 55.4%) had a full-time functional pathology department. Moreover, in most of the hospitals (34, 75.6%), more than 75% of patients had access to pathology. The pathology reports were, on average, available after 2.8 ± 1.7 weeks. Details are shown in Table 1.

Table 1
Descriptive statistics showing hospital characteristics and imaging and pathology facilities for breast cancer diagnosis in SSA hospitals SSA, 2018.

	Frequencies (n)	Percentage (%)
Population coverage (n = 47)		
< 50 000	10	21.3
50 000–199 999	4	8.6
200 000–499 999	2	4.3
500 000–999 999	9	19.2
1 000 000–1 999 999	5	10.6
Over 2 000 000	17	36.2
Type of hospital (n = 47)		
Nonreferral hospital	5	10.6
Referral hospital	42	89.4
Ultrasound availability (n = 47)		
On site and always available	36	76.6
On site but not working/available all the time	11	23.4
CT scan availability (n = 47)		
Not available at all	2	4.3
On site and always available	21	44.7
On site but not working/available all the time	12	25.5
Available at another hospital	12	25.5
Pathology services availability (n = 47)		
Not available	2	4.3
On site and always available	26	55.3
On site but not always available	4	8.5
Available at another hospital	15	31.9
Waiting time for pathology report in weeks (n = 45) *		
1	9	20.0
2	16	35.6

	Frequencies (n)	Percentage (%)
Population coverage (n = 47)		
3	8	17.8
4	9	20.0
8	3	6.7
Percentage of patients receiving pathology results (n = 45)		
<50%	2	4.4
50% – 75%	9	20.0
75% -100%	34	75.6

*The reports were, on average, available after 2.8 ± 1.7 weeks

Tumor boards

The MDT approach was reported in 33 hospitals (70.2%), and the treatment plan for cancer patients was systematically discussed in 9 hospitals (19.2%). Details are shown in Table 2.

Table 2
Descriptive statistics showing the availability of multidisciplinary teams (MDTs) for cancer patients in SSA hospitals, 2018, n = 47.

	Frequencies (n)	Percentages (%)
MDT availability		
Not available	14	29.8
Available only for some cancers	23	48.9
Available for all cancers treated in the hospital	10	21.3
Percentage of patient having MDT meeting		
None	3	6.4
10–50%	13	27.6
50–70%	6	12.8
80–90%	2	4.3
All patients	9	19.1
Not available	14	29.8

Among the specialties represented in the MDTs, surgeons were the most common attending physicians. In the majority of hospitals (n = 27), surgeons were available and present at more than 75% of MDTs. The most frequently missing physicians at MDTs were nurse oncology specialists, palliative care specialists, and medical/radiation oncologists. Details are shown in Table 3.

Table 3
Descriptive statistics showing the participation of cancer specialists in multidisciplinary team meetings in SSA hospitals, 2018, n = 47.

	Not available in the hospital (%)	Available but attends less than 75% of MDTs	Available in the hospital and attends more than 75% of MDTs	Missing
Oncologist	7 (14.9)	3 (06.4)	23 (48.9)	14 (29.8)
Radiologist	3 (6.4)	17 (36.2)	13 (27.7)	14 (29.8)
Pathologist	6 (12.8)	16 (34.0)	11 (23.4)	14 (29.8)
Specialist cancer nurse	19 (40.4)	6 (12.8)	8 (17.0)	14 (29.8)
Palliative care specialist	18 (38.3)	9 (19.2)	6 (12.8)	14 (29.8)
Surgeon	0 (0.0)	6 (12.8)	27 (57.5)	14 (29.8)

Adjuvant therapies (radiotherapy and chemotherapy)

In terms of adjuvant treatment to surgery, radiotherapy was available in nine hospitals (20.0%). It was inaccessible in the country of residence for patients attending ten of the 47 hospitals (nine hospitals without any access to radiotherapy and one hospital requiring patients to be transferred abroad for radiotherapy). When radiotherapy was available, the types of equipment used were both cobalt machines (n = 19, 40.4%) and linear accelerators (n = 19, 40.4%). Opioid pain medication was available in 51.1% (n = 24) of hospitals.

Most hospitals (n = 25, 53.2%) had chemotherapy drugs available on site. In nine hospitals (19.2%), patients had to travel more than 50 km to access chemotherapy drugs. Data on access to chemotherapy drugs are summarized in Table 4.

Table 4
Descriptive statistics showing the availability of radiotherapy, chemotherapy, surgery and opiate medication in SSA hospitals performing breast cancer surgery, 2018, n = 47

	Frequencies (n)	Percentages (%)
Radiotherapy availability		
Not available	9	19.2
Available in the hospital	8	17.0
Available at another hospital (within 10 km)	4	8.5
Available at another hospital (10–50 km)	11	23.4
Available at another hospital (> 50 km away)	14	29.8
Available in another country	1	2.1
Type of radiotherapy		
Cobalt accelerator	19	40.4
Linear accelerator	19	40.4
Not available	9	19.2
Availability of Chemotherapy drugs		
Not available	1	2.1
Available at the same hospital	25	53.2
Available at another hospital (within 10 km)	6	12.8
Available at another hospital (10–50 km)	6	12.8
Available at another hospital (> 50 km away)	9	19.2
Cash-payment of surgical care		
No patients make out of pocket payment	9	19.2
Yes - patients without insurance make out of pocket payments for at least part of their care	17	36.2
Yes - patients who can afford to are asked to make out of pocket payments for at least part of their care	6	12.8
Yes - all patients make out of pocket payments for at least part of their care	15	31.9
Availability of Postoperative care area		

	Frequencies (n)	Percentages (%)
Radiotherapy availability		
No	9	19.2
Yes – sometimes	6	12.8
Yes - all the time	32	68.1
Highest level of bed available		
Postoperative ward bed only	18	38.3
Specialist ward(s) providing intensive treatment and monitoring (HDU/ITU)	29	61.7
Acces to opiat pain medication		
Yes - but not always available	24	51.1
Yes - available all of the time	23	48,9

Hospitals providing optimal care for breast cancer patients

Only 14.9% (n = 7) of hospitals met the optimal criteria for diagnosis (Fig. 2A), and 10.6% (n = 5) of hospitals met the optimal criteria for treatment (Fig. 2B). Finally, only 6.4% of hospitals met all criteria for both diagnosis and treatment (Fig. 2C).

DISCUSSION

In this prospective, descriptive study of 47 hospitals equipped for the management of breast cancer patients in sub-Saharan Africa, differences in the ability of these facilities to provide a quality continuum of care for breast cancer patients were found.

Sub-Saharan Africa

SSA is, etymologically, the area of the African continent that lies south of the Sahara. According to the United Nations Population Division, the population is expected to grow rapidly by an annual average rate of 2.7% to reach 2.2 billion by 2050 [16].

Hospital size and coverage in SSA

More than one-third of the hospitals included in our study covered a population greater than two million people, and the majority were referral hospitals. These figures indicate that access to care is particularly

difficult for cancer patients in SSA. A study reported that more than one-sixth of the population in SSA lives more than two hours away from a public hospital [16].

Availability and access to breast cancer surgery in SSA

Our results indicate that surgeons are the most accessible specialists involved in breast cancer management in SSA. In most low-income countries, surgeons are often the only available specialists in cancer care and are responsible not only for diagnosis and surgical management but also for nonsurgical treatment (chemotherapy) as well as palliative care [17].

To improve the technical capacities of hospitals providing cancer care in SSA, there is clearly a need to train surgeons in a number of cancer surgical procedures [17]. In the US, the subspecialization of breast surgical oncology has resulted in more favorable outcomes and higher patient satisfaction [18].

Access to breast cancer imaging in SSA

Unlike CT, ultrasound was available in the majority of SSA hospitals covered by our study. The accuracy of ultrasonography in the preoperative assessment of breast cancer is necessary to provide accurate loco-regional pretreatment planning [19], but CT is essential for disease staging and the extension workout. In most SSA countries, clinical examination, chest radiography, and ultrasound are often the only available resources for staging a patient [17].

Access to pathology in SSA

Only half of the hospitals in this study had a functional full-time pathology department. Breast cancer management is based on pathology and immunohistochemistry findings [20]. In most low-resource settings, such as SSA, patients with breast cancer rarely obtain a histological diagnosis; therefore, many receive inappropriate treatment [17]. The greatest challenge in most LMICs is the lack of human resources [17, 20]. In SSA, for instance, there are less than 80 pathologists for every 1 million population (60 times less than recommended) [17].

Access to radiotherapy

Access to radiotherapy is probably the most challenging aspect of breast cancer management in SSA. In fact, SSA is the region of the world with the most limited radiotherapy services [21]. In 2017, twenty-nine African countries out of fifty-four reported having no access to radiation services [5]. In our study, radiotherapy was one of the least available therapies. The 2020 WHO World Cancer Report highlighted data showing the significant relationship between the number of available radiotherapy machines and cancer mortality [22]. The limited access to radiotherapy could explain, in part, the excess mortality from breast cancer in SSA for several reasons. First, the majority (up to 90% in some countries) of breast cancers are diagnosed at a late stage in SSA [5], and radiotherapy is a pivotal treatment for the control of locally advanced breast cancers. Radiotherapy can also have an impact on the acceptability of care. Indeed, in a study conducted in Nigeria [23], fear of mastectomy was the primary cause of delay in the management of women with breast cancer. African series are characterized by a high rate of mastectomy

compared to Western series due, among other things, to the absence of radiotherapy, which is the standard of postsurgical care in cases of breast-conserving surgery.

Even when radiotherapy was available, the devices sometimes do not comply with international recommendations (half of the hospitals in our study still use a cobalt accelerator, which is considered to be less appropriate than a linear accelerator). Cobalt accelerators are suboptimal for radiotherapy treatment, particularly in SSA, for many reasons. First, cobalt's decaying dose rate and its more significantly reported grade 3 to 5 toxicities limit its use in clinical situations compared with linear accelerators. Moreover, there are security concerns with that active source, which always produces radiation, has a high potential for harm and requires specific security measures for source transfers, disposal and the vault that hosts the unit [24].

Another issue is the fact that the devices sometimes fail, resulting in dramatic situations. In a previous study, the radiotherapy machine at one of Uganda's main cancer centers was down for 18 months; therefore, only 15% of patients with breast cancer had access to radiotherapy [4].

Access to chemotherapy and systemic therapies

Breast cancer in Africa is thought to be a more aggressive disease occurring in younger women with poor hormone receptor staining, which may require the use of many lines of chemotherapy [5]. Moreover, with most breast cancer patients presenting at late stages in SSA, the role of surgery as a curative measure is reduced [6].

In our study, only half of the hospitals (n = 25, 53.1%) had chemotherapy drugs available on site. Unfortunately, even when chemotherapy is offered, experience has shown that the limited availability and cost of treatment lead to high rates of interruption and premature termination of cycles [6]. In Eritrea, in 2013, more than 97% of patients received surgical intervention as their only treatment because there were no chemotherapy or radiotherapy options available nationally [6, 25].

Nevertheless, chemotherapy is cost prohibitive for most patients on the African continent [5]. The discovery of HER 2-targeted therapy, such as trastuzumab or pertuzumab, and more recently immunotherapy, such as pembrolizumab, has revolutionized the management of certain subtypes of breast cancer. However, despite the inclusion of some of those systemic therapies in the World Health Organization (WHO) essential drug list, the cost of these life-saving drugs remains, unfortunately, high [5] and therefore inaccessible for most patients in SSA. Tamoxifen, a very low-cost hormonal therapy sometimes available free of charge, is one of the most accessible treatment options even in poorer countries of SSA. Unfortunately, in black women, the most common type of breast cancer seems to be triple-negative breast cancer, which is known to be much more aggressive and less sensitive to hormonal therapies [26].

MDT

Our study found that MDTs are not available in most hospitals treating breast cancers in SSA. Moreover, even when MDTs were available, only a limited proportion of patients, which varies greatly from one hospital to another, were discussed. This could partially explain the excess breast cancer mortality in SSA. In some settings, MDT care was reported to intercept 98.8% of all medication errors and improve the quality of care [27]. In the United Kingdom, for example, the introduction of MDTs and the resulting improvement of processes and treatment pathways has reduced breast cancer mortality by 18.0% [8].

One of the most important aspects of MDT care is the quality and variety of team members. In breast cancer services in the UK, at a minimum, the MDT core members for breast cancer care include clinical and medical oncologists, breast surgeons, radiologists, pathologists and breast care nurse specialists [27]. In our study, the most frequently missing practitioners at MDTs were nurse oncology specialists. In a previous report, MDT members identified specialist oncology nurses as “the glue of the team” [28].

Access to palliative care and opiate prescriptions

According to our study, access to opiate pain medication seems to be low. It is astonishing that such a relatively inexpensive, essential medicine is inaccessible to the world's poorest region [29]. According to a scoping review of palliative care in Africa [30], the limited availability of opioids in Africa is because some countries have strict regulations on opioid use and prescription, while others require specific licenses to prescribe or administer morphine. At a hospital level, training in pain management and the presence of a palliative care team could improve morphine prescription [31].

Pathway and financial access to care

The pathways that patients take to breast cancer treatment in SSA are numerous and littered with obstacles because of both patient- and system-related factors. In addition to diagnostic delays that we have already discussed, there are further delays between confirmation of diagnosis and onset and completion of therapy [2, 32]. Understanding these barriers would support global and country-level decision-makers in planning and programmes for improvements [33].

Limitations of the study

Although we examined 47 hospitals from 15 countries, we cannot ensure that our sample is representative of all hospitals treating breast cancer in SSA. However, this work produces estimates of the availability and quality of breast cancer treatment that were not previously estimated from SSA to the best of our knowledge. Our study produces estimates from data collected in the field and could be used to inform public health authorities on breast cancer management in SSA and to improve models for access to breast cancer treatment in SSA.

CONCLUSION

We obtained information on breast cancer management services from 47 hospitals, 15 countries and 43 cities in SSA and found inequities in access to breast cancer care in the region. Improving breast cancer

survival in sub-Saharan Africa (SSA) is an emergency that cannot be challenged without the strengthening of hospital infrastructure and resources [14]. These results also show that a strategy of strengthening hospital capabilities in SSA could markedly reduce breast cancer-related mortality.

Because surgery is a key component of breast cancer patient management, focusing on it as part of national cancer control plans is crucial to reduce the premature mortality from breast cancer observed in SSA [17]. Finally, addressing inequities in breast cancer treatment will be essential in meeting gender equality Sustainable Development Goals, as well as health and wellbeing objectives [4].

Abbreviations

ABC-DO: African Breast Cancer - Disparities in Outcomes cohort study

CT: Computed tomography

HDI: human development index

HER2: Human epidermal growth factor receptor 2

HIV: Human immunodeficiency virus.

IHC: Immunohistochemistry

MDT: Multidisciplinary Team

MRI: Magnetic resonance imaging

NIHR: National Institute for Health Research

REDCap: Research Electronic Data Capture system.

SSA: sub-Saharan Africa

UN: United Nations

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Since the Globalsurg3 project does not affect clinical practice and patient outcome, it has been classified as a clinical audit by the UK National Health Service (NHS) Research Ethics proportionate review and exempted from formal research registration (South East Scotland Research Ethics Service, reference NR/161AB6)[8]. Individual centers obtained their own audit or institutional approval, together with ethical

approval as per local regulations. Informed consent was obtained from all participants. The study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Consent for publication

No applicable

Data availability statement

Data for this study contain confidential patient information. The data sets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests

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Author contributions:

HE and PMP conceived the idea for the study.

GFHR, LI, KS, and FMD designed the research and analyzed the data.

GFHR and TT performed statistical analyses.

GFHR and KS drafted the manuscript.

GFHR, LI, KS, PA, DFM, TT, HSD, BV, PMP, SRK and HE critically reviewed the manuscript and approved the final version.

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Authors' information

No applicable

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Figures

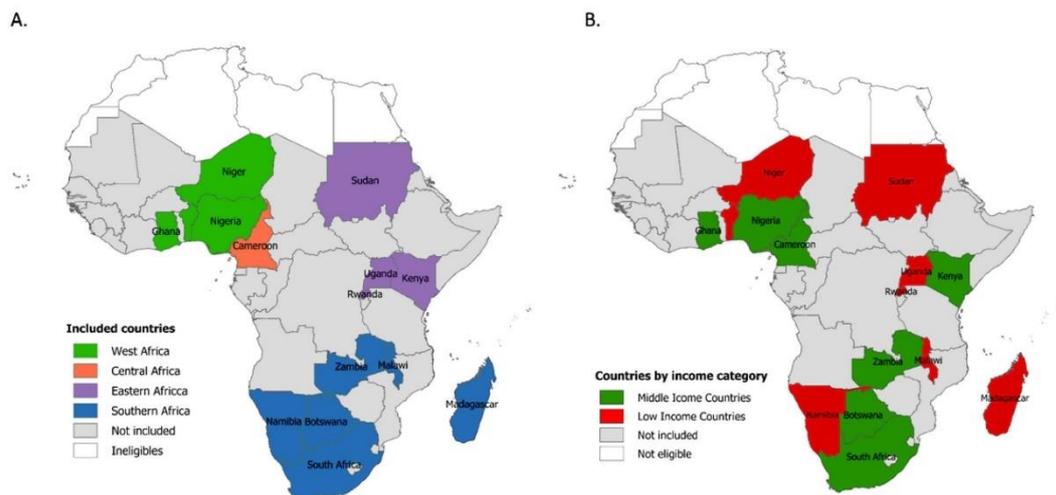


Figure 1

SSA countries included in our study. A) Map showing the geographic distribution of SSA countries included in the study, 2018, n=15. **B)** Map showing the distribution of SSA countries included in the study according to income category, 2018, n=15

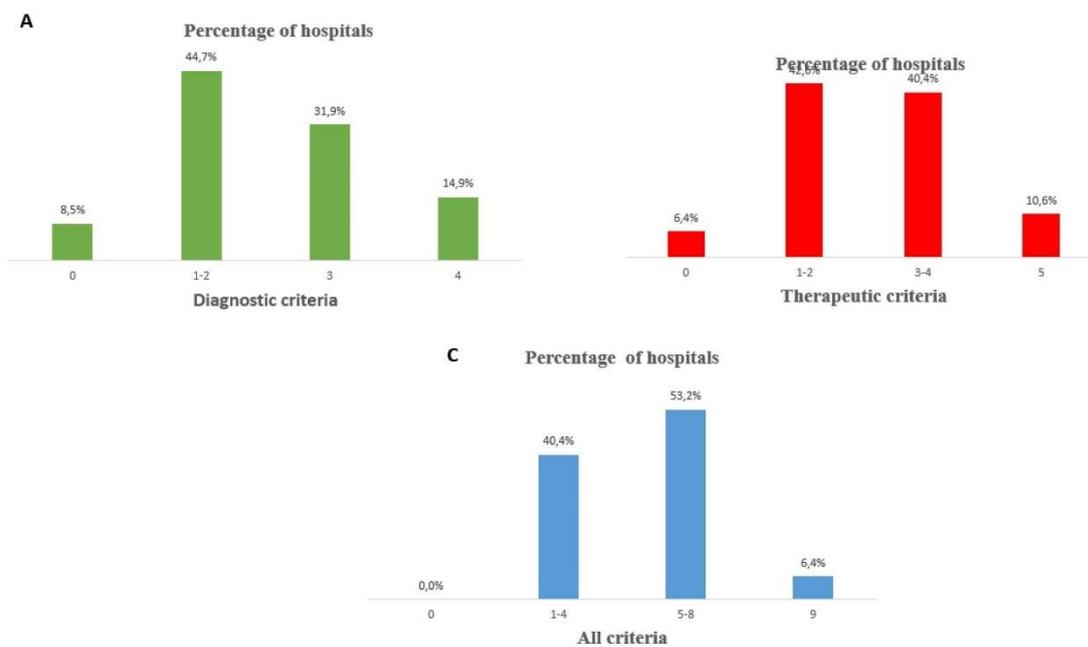


Figure 2

Percentage of hospitals providing optimal care **A)** Diagnostic criteria **B)** Therapeutic criteria **C)** All criteria

Supplementary Files

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III.3. Conformité des formulaires de demande et des comptes rendus anatomopathologiques de pièces opératoires de cancer du sein au Bénin

Le cancer du sein requiert une prise en charge pluridisciplinaire. Les difficultés de communication sont les facteurs contribuant à la plupart des erreurs médicales entraînant un préjudice parfois mortel pour le patient ; lorsqu'elles n'en sont pas la principale cause. Les anatomopathologistes et les médecins impliqués dans la prise en charge du cancer du sein communiquent grâce au formulaire de demande et au compte rendu d'examen anatomopathologique. Il est donc crucial que ces documents soient bien rédigés pour permettre, d'une part aux anatomopathologistes d'effectuer un diagnostic précis des cancers et une évaluation optimale des facteurs pronostiques, d'autre part aux médecins oncologues de prendre les décisions adéquates. Dans les pays développés, les études sur le sujet sont nombreuses et la tendance est à la standardisation de ces documents. Cependant, il n'est pas toujours possible d'obtenir certaines de ces données dans les pays à faible revenu comme ceux d'Afrique subsaharienne.

Le but de ce travail était d'évaluer la complétude des formulaires de demande et des comptes rendus d'examen anatomopathologique de pièces opératoires de cancers du sein chez les femmes au Sud du Bénin. Une collecte rétrospective de données sur 57 mois (4 ans et 9 mois) a été faite ; nous avons utilisé les recommandations de la Haute Autorité de Santé de France comme référentiel et le logiciel SPSS pour traiter les données. Les formulaires de demande étaient conformes aux recommandations dans 31,3% des cas. Les comptes rendus étaient narratifs dans 92,7 % des cas et 68,8 % comportaient les critères minimaux.

Nous concluons que les chirurgiens et les anatomopathologistes impliqués dans la prise en charge des cancers du sein au Bénin ne rédigent pas toujours entièrement les formulaires de demande et les comptes rendus d'examen anatomopathologique. Ceci peut s'expliquer par l'absence de référentiels nationaux, et les difficultés d'accès à l'immunohistochimie. L'élaboration de référentiels nationaux, l'utilisation de comptes rendus synoptiques et la mise en place d'un cadre de concertation adapté pourraient améliorer les pratiques.

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CANCÉROLOGIE/ONCOLOGY

Conformité des formulaires de demande et des comptes rendus anatomopathologiques de pièces opératoires de cancer du sein au Bénin

Adequacy of histopathology request forms and pathological reports of breast cancer surgical specimens in Benin

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RÉSUMÉ **Introduction.** Le cancer du sein requiert une prise en charge pluridisciplinaire. Les anatomopathologistes et les médecins communiquent grâce au formulaire de demande et au compte rendu d'examen anatomopathologique. Il est crucial que ces deux documents soient bien rédigés pour une bonne prise en charge des patientes.

Objectif. Évaluer la complétude des formulaires de demande et des comptes rendus d'examen anatomopathologique de pièces opératoires de cancers du sein chez les femmes au Sud du Bénin.

Méthode. Il s'agissait d'une étude transversale, descriptive et analytique, avec une collecte rétrospective de données sur 57 mois (4 ans et 9 mois). Nous avons utilisé les recommandations de la Haute Autorité de Santé de France comme référentiel et le logiciel SPSS pour traiter les données.

Résultats. 31,3 % des formulaires de demande étaient conformes aux recommandations. Les comptes rendus étaient narratifs dans 92,7 % des cas et 68,8 % comportaient les critères minimaux. La présence d'embolies vasculaires, le statut HER2 et les récepteurs hormonaux étaient tous simultanément renseignés dans seulement 29,2 % des comptes rendus. La présence d'embolies vasculaires était le facteur pronostique le plus souvent renseigné.

Discussion. Les chirurgiens et les anatomopathologistes ne rédigent pas toujours entièrement les formulaires de demande et les comptes rendus d'examen anatomopathologique. Ceci peut s'expliquer par l'absence de référentiels nationaux, et les difficultés d'accès à l'immunohistochimie. L'élaboration de référentiels nationaux et l'utilisation de comptes rendus synoptiques pourraient améliorer les pratiques.

Mots clés: Cancer du sein, Chirurgie oncologique, Conformité, Formulaire de demande d'examen, Compte rendu d'examen anatomopathologique, Bénin, Afrique subsaharienne

ABSTRACT **Introduction.** Breast cancer requires multidisciplinary management. Pathologists and physicians communicate using the histopathology request form and the pathology report. There are some minimal criteria that both should respect.

Objective. We assessed the adequacy of histopathology request forms and pathology reports in the management of female breast cancer specimens in Southern Benin.

Method. This was a cross-sectional, descriptive and analytical study, with retrospective data collection over 57 months (4 years and 9 months). The adequacy of the histopathology request forms and pathology reports was assessed on the basis of the recommendations of the

Haute Autorité de Santé (HAS) of France. Data processing was done using SPSS software. We checked frequencies with the Chi² test, with a significance level set at 5%.

Results. 31.3% of histopathology request forms complied with HAS recommendations. Pathology reports were presented in a narrative way in 92.7% of cases and 68.8% met the minimal criteria. The presence of vascular embolus, of hormone receptors and the HER2 status were all reported in only 29.2% of the reports.

Discussion. The draft of histopathology request forms and pathology reports did not comply to the required minimal criteria. This situation could mainly be explained by the inexistence of consensus between physicians and pathologists and by the lack of immunohistochemistry. Editing national referentials and using synoptic reports would give better results.

Keywords: Breast cancer, Surgical oncology, Adequacy, Pathology request form, Histopathology report, Benin, Sub-Saharan Africa

Introduction

Avec plus de 2 millions de nouveaux cas et plus de 600 000 décès en 2020, le cancer du sein est un problème majeur de santé publique à l'échelle mondiale [26]. La situation semble encore plus préoccupante en Afrique subsaharienne. En effet, bien que l'incidence y soit parmi les plus faibles au monde, la mortalité y est la plus élevée.

Au Bénin, pays d'Afrique de l'Ouest, le cancer du sein est le premier cancer de la femme aussi bien en termes d'incidence que de mortalité [26]. Les raisons le plus souvent évoquées pour expliquer la surmortalité sont le diagnostic tardif et le faible accès aux traitements, mais également les dysfonctions du système de santé [15].

Le diagnostic de certitude et l'évaluation du pronostic du cancer du sein reposent sur l'examen anatomopathologique. Sa prise en charge se veut multidisciplinaire. La chirurgie est la pierre angulaire de ce traitement, particulièrement dans les pays en voie de développement où l'accès aux thérapies systémiques et à la radiothérapie peut se révéler problématique. En outre, l'information apportée par la pièce d'exérèse chirurgicale est capitale pour déterminer la prise en charge médicale et/ou radiothérapique adjuvante. Parallèlement, la complexité toujours croissante du traitement du cancer du sein, y compris le traitement chirurgical, exige un processus de diagnostic de haute qualité, dans lequel l'anatomie pathologique joue un rôle central.

Les chirurgiens et médecins oncologues d'une part, et les anatomopathologistes d'autre part, communiquent de manière formelle essentiellement au travers de deux documents : les formulaires de demande d'examen anatomopathologique (FDA) et les comptes rendus d'examen anatomopathologique (CRA). Les informations contenues dans le FDA relèvent du médecin préleveur (le chirurgien) et sont cruciales pour la bonne conduite de l'examen anatomopathologique. De même, les informations contenues dans les CRA de pièces opératoires sont d'une importance capitale pour le choix du traitement locorégional et systémique adjuvant et l'estimation du pronostic [5,13,14].

Il est donc crucial que ces documents soient bien rédigés pour permettre, d'une part aux anatomopathologistes d'effectuer un diagnostic précis des cancers et une évaluation optimale des facteurs pronostiques, d'autre part aux médecins oncologues de prendre les décisions adéquates. Les difficultés de communication sont les facteurs contribuant à la plupart des erreurs médicales entraînant un préjudice pour le patient ; lorsqu'elles n'en sont pas la principale cause.

Dans les pays développés, les études sur le sujet sont nombreuses et la tendance est à la standardisation de ces documents [12,25].

En France, la Haute Autorité de Santé (HAS) a édité des recommandations sur les données minimales à renseigner dans un CRA [29]. Cependant, il n'est pas toujours possible d'obtenir

certaines de ces données dans les pays à faible revenu comme ceux d'Afrique subsaharienne. De plus, certaines de ces informations peuvent ne pas être pertinentes au vu des moyens thérapeutiques disponibles dans ces pays [31]. Par conséquent, des instances internationales telles que la Breast Cancer Initiative 2.5 (BCI 2.5) ont stratifié les recommandations en fonction des contextes et des ressources disponibles dans chaque pays (ressources de santé de niveau basique, moyen, amélioré et maximal) [2,10,20].

En Afrique subsaharienne, à notre connaissance, peu d'études ont évalué les pratiques des chirurgiens et des anatomopathologistes dans la rédaction de ces documents. De plus, au Bénin, il n'existe pas de recommandations nationales concernant la présentation des FDA et des CRA.

Notre objectif est d'évaluer la complétude des données renseignées dans les FDA et les CRA des pièces opératoires des patientes prises en charge pour un cancer du sein dans deux hôpitaux de référence au Bénin.

Cadre et méthode d'étude

Type d'étude, cadre et population

L'étude était transversale, descriptive et analytique, avec une collecte rétrospective des données. Elle a intéressé les FDA et les CRA de pièces opératoires de cancer du sein histologiquement confirmé, édités entre le 1^{er} janvier 2015 et le 30 septembre 2020. La structure des FDA différait en fonction des services ; de même, la structure des CRA différait en fonction des laboratoires et du pathologiste qui les rédigeaient. Ces documents étaient établis par les équipes médicales de chacune de ces structures.

Nous avons effectué une étude multicentrique incluant deux hôpitaux de référence à l'échelle nationale dans la prise en charge des cancers du sein, situés à Cotonou (capitale économique du Bénin) :

- Centre national hospitalier universitaire Hubert Koutoukou Maga (CNHU-HKM)
- Centre hospitalier universitaire de la mère et de l'enfant Lagune (CHU-MEL)

Les observations médicales de patientes ayant un cancer du sein histologiquement confirmé et ayant bénéficié d'une chirurgie mammaire, conservatrice ou radicale, et pour lesquelles un CRA était disponible, ont été recensées dans un premier temps. Les FDA correspondants étaient ensuite recherchés dans les laboratoires d'anatomie pathologique desservant ces hôpitaux de référence. Il s'agissait d'un laboratoire public – le laboratoire d'anatomie pathologique et de cytologie de la Faculté des sciences de la santé (LAPC-FSS) – et de trois laboratoires privés – le laboratoire d'anatomie pathologique et de cytologie du Centre Adéchina/Clinique Dubois (CAAP), le laboratoire d'anatomie pathologique du cabinet médical Foi en Dieu et le laboratoire d'anatomie pathologique du Centre confessionnel Padre Pio. Tous les laboratoires étaient situés dans la ville de Cotonou.

Les FDA et CRA de biopsie ont été exclus.

Variables

Dans un premier temps, la complétude des formulaires de demande et des comptes rendus d'examen anatomopathologique a été évaluée, selon les recommandations de la HAS de France. Seul l'aspect quantitatif a été évalué. Les critères de la HAS sont répartis en deux groupes [29] :

• Description de la pièce opératoire

Elle est sous la responsabilité du médecin préleveur (le chirurgien). Cette description comprend quatre éléments qui ne peuvent être renseignés par le pathologiste et qui lui ont été transmis par le chirurgien. Nous avons donc recherché ces éléments, directement dans les FDA transmis par les chirurgiens aux différents laboratoires d'anatomie pathologique. Ces éléments sont :

1. la latéralité du sein ;
2. la localisation de la tumeur dans le sein ;
3. la technique chirurgicale employée ;
4. l'orientation de la pièce opératoire.

• Description histopathologique

Elle a directement été recherchée dans les CRA. Cinq éléments doivent être renseignés au minimum selon les recommandations de la HAS [29] :

1. le type histologique [17] ;
2. le grade histopronostique [9] ;
3. l'extension tumorale (marge d'exérèse, existence de foyers infiltrants multiples) [29] ;
4. les critères permettant de déterminer le pT/pN (statut des ganglions axillaires) [17] ;
5. les autres facteurs pronostiques et /ou prédictifs :
 - embolies vasculaires [29] ;
 - statut des récepteurs hormonaux (œstrogènes et progestérone) par immunohistochimie [29] ;
 - statut HER2 par immunohistochimie [29] ;
 - réponse histologique après traitement néo-adjuvant [23].

Nous avons par ailleurs distingué deux types de mode de présentation des CRA :

- CRA narratifs
- CRA synoptiques

Étaient considérés comme synoptiques, les CRA contenant un tableau synthétique présentant les résultats de l'examen [4]. Tous les autres étaient considérés comme narratifs.

Dans un second temps, les CRA ont été répartis en trois groupes selon la classification du Breast Cancer Initiative 2.5 qui classe les outils employés dans la prise en charge du cancer du sein en quatre niveaux [1,2,18,24]. Ainsi avons-nous distingué, en ce qui concerne le diagnostic :

- les analyses de niveau basique regroupant des éléments qui devraient être renseignés dans tous les CRA quel que soit le niveau de ressources dont dispose le système sanitaire. Il s'agissait : du type histologique, du grade SBR et de la classification pT/pN [8,10].
- les analyses de niveau moyen regroupant des éléments qui peuvent être renseignés en utilisant des ressources limitées mais qui induisent une amélioration majeure de la prise en charge. Il s'agit de l'évaluation des marges, de la recherche d'embolies

lymphovasculaires et de la recherche des récepteurs aux œstrogènes [8,10].

- les analyses de niveau amélioré regroupant des éléments qui nécessitent des ressources importantes et qui produisent une amélioration de la prise en charge. Il s'agit de la recherche des récepteurs à la progestérone et HER2 [8,10].

La Breast Cancer Initiative 2.5 définit un quatrième niveau d'outils, les « analyses de niveau maximal », qui n'est pas pertinent pour cette étude réalisée dans un pays à ressources limitées où l'accès à certaines options thérapeutiques de dernière génération est impossible [21].

Analyse statistique

La comparaison des fréquences a été réalisée avec le test de Chi² lorsque les effectifs théoriques étaient supérieurs ou égaux à 5. Lorsque les conditions d'application n'étaient pas remplies, le test de Fischer a été utilisé. Le seuil de significativité des tests statistiques a été fixé à 5 %. Le traitement des données a été réalisé à l'aide du logiciel SPSS version 26.0.

Résultats

Durant la période d'étude, 147 patientes ont bénéficié d'une chirurgie pour cancer du sein dans les deux centres de référence. Les observations médicales de 51 d'entre elles (35 %) ne remplissaient pas les critères d'inclusion. Finalement, 96 observations médicales ont été considérées pour l'analyse finale (Fig. 1). L'âge moyen des patientes au moment du diagnostic était de 49,2 ans avec un écart-type de 11 ans. Le pic de fréquence était observé entre 40 et 50 ans (Fig. 2). L'intervention chirurgicale la plus réalisée était la mastectomie radicale associée à un curage axillaire (n = 61 ; 63 %). La majorité des pièces opératoires étaient orientées (n = 68 ; 71 %) avec des marges saines (n = 78 ; 81 %) à l'analyse histopathologique. Le type histologique prédominant était le carcinome infiltrant de type non spécifique (n = 88 ; 92 %). Les caractéristiques générales des 96 pièces opératoires sont détaillées dans le Tableau I.

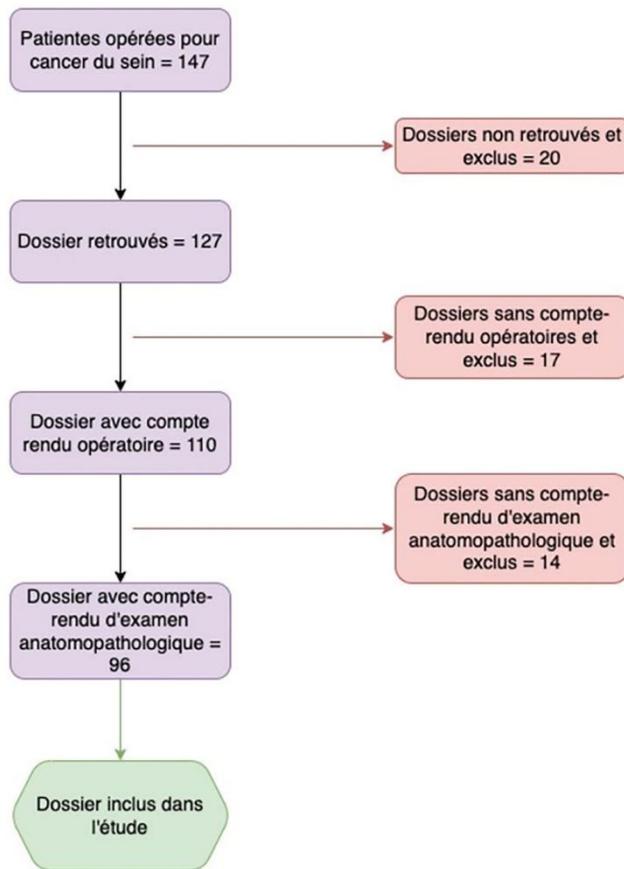


Figure 1 : Organigramme de l'étude
Figure 1: Flow-chart of the study

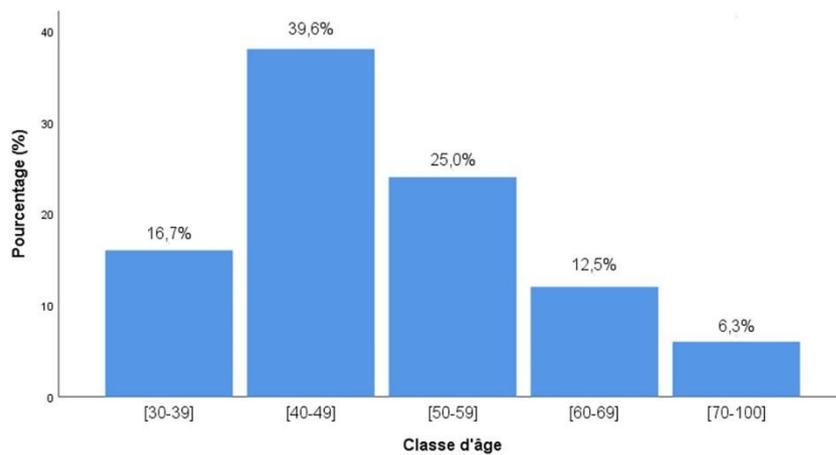


Figure 2 : Répartition des patientes en fonction de l'âge au diagnostic (n = 96)
Figure 2: Distribution of patients by age at diagnosis (n = 96)

Tableau I : Caractéristiques générales des pièces opératoires de cancer du sein
Table I: General characteristics of breast cancer surgical specimen

Caractéristiques	Fréquence	%
Sein atteint		
droit	52	54,1
gauche	40	41,7
bilatéral	0	0,00
non documenté	4	4,2
Quadrant du sein atteint		
central	1	1,0
quadrant supéro-externe	11	11,5
quadrant supéro-interne	1	1,0
quadrant inféro-interne	2	2,1
quadrant inféro-externe	6	6,3
multiples	20	20,8
non documenté	55	57,3
Curage axillaire		
au moins 10 ganglions	61	63,5
moins de 10 ganglions	17	17,8
non réalisé	18	18,7
Type histologique		
carcinome canalaire in situ	1	1,0
carcinome infiltrant de type non spécifique	88	91,7
carcinome lobulaire infiltrant	2	2,1
carcinome mucineux	1	1,0
réponse histologique complète	4	4,2
non documenté	0	0,00
Grade SBR		
I	13	13,5
II	44	45,8
III	33	34,4
non documenté	6	6,3
Récepteur aux œstrogènes		
négatif	20	20,8
positif	21	21,9
non documenté	55	57,3
Récepteur à la progestérone		
négatif	27	28,1
positif	14	14,6
non documenté	55	57,3

Statut HER2		
négatif	35	36,4
positif	6	6,3
non documenté	55	57,3
Embole lymphovasculaire		
absent	53	55,2
présent	14	14,6
non documenté	29	30,2
Taille de la tumeur T selon la classification pTNM		
pT0	3	3,1
pT1	8	8,3
pT2	31	32,3
pT3	15	15,6
pT4	6	6,3
non documenté	33	34,4
Ganglions N selon la classification pTNM		
pN0	25	26,1
pN1	15	15,6
pN2	12	12,5
pN3	5	5,2
pNx	1	1,0
non documenté	38	39,6
Marges		
saines	78	81,2
atteintes	12	12,5
non documenté	6	6,3
Type de compte rendu		
narratif	89	92,7
synoptique	7	7,3

Formulaire de demande d'examen anatomopathologique

La situation de la tumeur dans le sein était l'élément le moins souvent renseigné (n = 41 ; 43 %). L'élément le plus souvent renseigné était la latéralité du sein (n = 92 ; 96 %). La Figure 3 résume la fréquence des principaux critères sur les FDA.

Compte rendu d'examen anatomopathologique

Mode de présentation

Les CRA étaient narratifs dans 93 % (n = 89) des cas. Nous avons retrouvé 7 comptes rendus synoptiques soit 7 %.

Éléments renseignés

Conformément aux critères d'inclusion, un type histologique était présent sur tous les comptes rendus sauf pour 4 patientes (4,2 %) qui avaient présenté une réponse histologique complète sans doute suite à une chimiothérapie néo-adjuvante. La marge (n = 92 ; 96 %) était le critère le plus souvent renseigné par les pathologistes sur les CRA, suivi du grade histopronostique selon la classification de Scarff Bloom Richardson (n = 90 ; 94 %). Les critères explorés par l'immunohistochimie (récepteurs aux œstrogènes, récepteurs à la progestérone, surexpression du HER2) étaient les critères les moins souvent renseignés (Fig. 4).

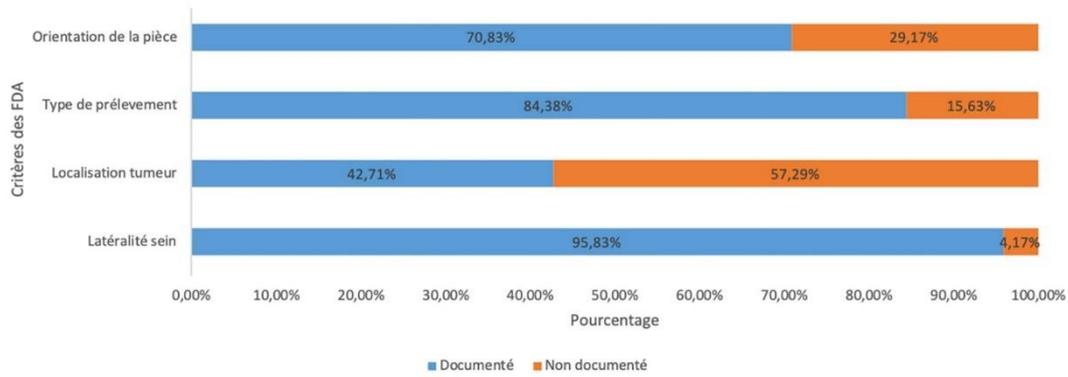


Figure 3 : Fréquence d'apparition des différents critères minimaux sur les formulaires de demande d'examen anatomopathologique (n = 96)

Figure 3: Frequency of minimal criteria on histopathology request forms (n = 96)

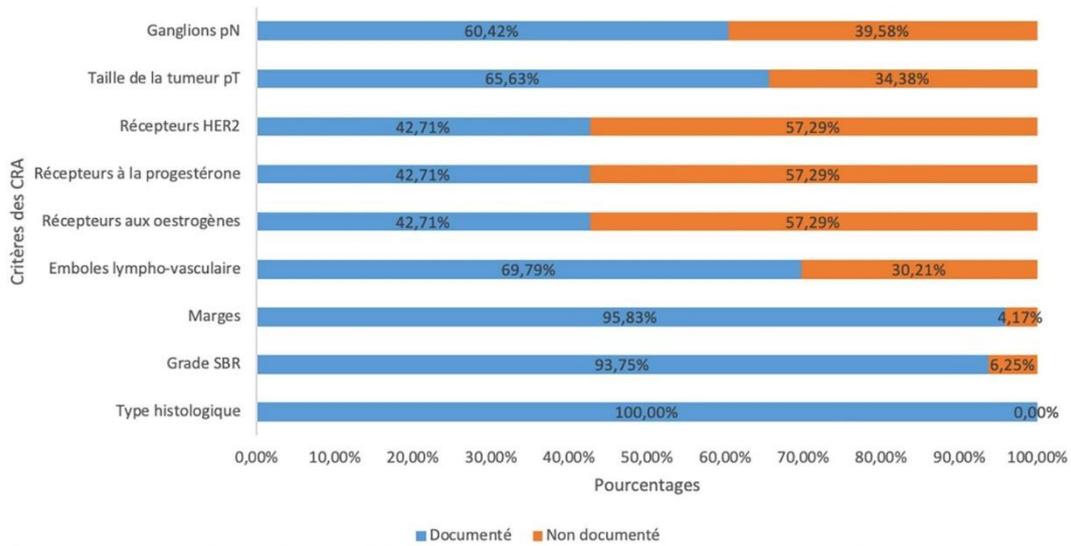


Figure 4 : Fréquence d'apparition des différents critères minimaux sur les comptes rendus d'examen anatomopathologique (n = 96)

Figure 4: Frequency of minimal criteria on pathology reports (n = 96)

Tableau II : Répartition des fréquences de renseignement des critères minimaux selon le type de compte rendu
Table II: Distribution of the frequencies of minimal criteria according to report type

	Type de compte rendu				
	Narratif (n=89)		Synoptique (n=7)		P
	Fréquence	%	Fréquence	%	
Analyses de niveau basique					
taille de la tumeur T	60	67,4	7	100	0,071
ganglions N	63	70,8	7	100	0,094
type histologique	83	100	7	100	
grade SBR	83	93,3	7	100	0,478
1 élément présent	2	2,2	0	0	NA
2 éléments présents	24	27	0	0	NA
3 éléments présents	7	7,9	0	0	NA
4 éléments présents	56	62,9	7	100	NA
Analyses de niveau moyen					
récepteurs aux œstrogènes	34	38,2	7	100	0,001
emboles lymphovasculaires	61	68,2	6	85,7	0,402
marges	85	95,5	7	100	0,567
0 élément présent	3	3,4	0	0	NA
1 élément présent	15	16,9	0	0	NA
2 éléments présents	48	53,9	1	14,3	NA
3 éléments présents	23	25,8	6	85,7	NA
Analyses de niveau amélioré					
statut HER2	34	38,2	7	100	0,001
récepteurs à la progestérone	34	39,5	7	100	0,001

NA : Non applicable

En ce qui concerne la présentation, les CRA synoptiques renseignaient plus souvent les critères immunohistochimiques (récepteurs à l'œstrogène, récepteurs à la progestérone, surexpression du HER2) que les CRA narratifs. Cette différence était statistiquement significative ($p < 0,05$). Le Tableau II résume la répartition des éléments renseignés (narratif/synoptique) en fonction du type de CRA.

Discussion

Intérêt et limites de l'étude

Cette étude sur la complétude des FDA et des CRA de pièces opératoires de cancer du sein dans deux hôpitaux de référence du Bénin a mis en évidence une discordance entre les pratiques et les recommandations pour un pays à faibles ressources comme le Bénin.

Toutefois, notre étude présente des limites. D'une part, réalisée dans deux hôpitaux publics de référence à l'échelle nationale situés dans le Sud du Bénin, elle n'est pas représentative de la situation dans tous les hôpitaux du pays, notamment les centres publics du Nord du pays et les centres privés. D'autre part, les insuffisances dans le processus d'archivage nous ont contraints à exclure les observations de certaines patientes. Ceci a considérablement réduit la taille de notre échantillon, diminuant la puissance statistique de notre étude.

Malgré ces limites, notre étude revêt un intérêt certain. En effet, dans les pays développés, de nombreuses études ont évalué l'exhaustivité des renseignements contenus dans les CRA de pièces opératoires de cancer du sein et ont par conséquent permis de faire des recommandations qui ont abouti à une meilleure rédaction de ces documents [4,6,12,16,19,22,25,30].

En Afrique subsaharienne, par contre, peu d'études ont été réalisées. À notre connaissance, seules trois études publiées ont décrit des audits similaires. Ces trois études ont identifié des lacunes importantes dans le renseignement des informations provenant des analyses du niveau basique du BCI 2.5 sur les FDA et les CRA [3,7,31]. Autant que nous le sachions, notre étude est la première au Bénin à évaluer les FDA et CRA dans les cancers du sein. Elle pourra servir de référence pour la réalisation d'études plus importantes.

Formulaire de demande d'examen anatomopathologique

Nous avons déterminé que seulement 31 % des FDA contenaient l'ensemble des quatre renseignements minimaux requis par la HAS. L'absence de ces renseignements peut influencer sur le délai et la qualité de l'examen anatomopathologique, notamment en ce qui concerne l'orientation de la pièce opératoire et la localisation de la tumeur dans le sein. En effet, en l'absence de ces renseignements, le pathologiste doit recontacter le médecin préleveur avant de procéder à l'examen. Dans notre contexte où les pathologistes sont surchargés, car peu nombreux [11], ces situations contribuent à prolonger le délai de rendu des résultats. Nos résultats sont similaires à ceux obtenus par Vallacha *et al.* à Karachi (Pakistan), qui ont trouvé 34 % de FDA contenant les quatre critères minimaux [28]. En revanche, Barré *et al.*, dans une étude prospective, ont retrouvé au CHU de Nantes que 69 % des FDA étaient complets. L'élément le moins souvent renseigné dans cette étude était la technique chirurgicale utilisée [6]. Les différences entre nos résultats et ceux de Barré *et al.* pourraient s'expliquer par les différences de méthodologie, et surtout par le fait que le FDA utilisé dans le CHU de Nantes était un formulaire prérempli, plus facile à renseigner.

Compte rendu d'examen anatomopathologique

L'absence de certains renseignements dans un CRA de pièce opératoire peut induire une décision inadéquate pour le choix du traitement adjuvant. Ainsi, l'absence d'information

sur les récepteurs hormonaux sur le CRA prive d'emblée les patientes de l'accès à l'hormonothérapie dans le cas, plutôt fréquent, où la recherche des récepteurs hormonaux n'a pas été effectuée sur la pièce de biopsie initiale. Nous avons remarqué une grande variabilité dans la fréquence des différents critères présentés dans les comptes rendus d'examen anatomopathologique. Globalement, les éléments fournis par une analyse histologique standard étaient plus souvent renseignés que ceux nécessitant l'usage de techniques spéciales comme l'immunohistochimie (Tableau II). Cela s'explique en partie par l'indisponibilité de ces examens dans notre contexte. En effet, grâce à une étude menée entre 2011 et 2014, Nelson *et al.* ont montré que seulement 53 % des pays d'Afrique subsaharienne disposaient de l'immunohistochimie et que les techniques de biologie moléculaire n'étaient disponibles que dans deux pays [21]. Dans notre étude, seules les femmes qui avaient les moyens d'assurer l'envoi de l'échantillon à l'extérieur (en France notamment) ont bénéficié d'une analyse immunohistochimique complète de leur prélèvement. Ce constat soulève la problématique de l'accès au diagnostic et au traitement du cancer du sein en Afrique subsaharienne. Dans les pays développés, les critères relatifs à l'analyse immunohistochimique sont renseignés dans plus de 90 % des cas [4,27].

Analyses de « niveau basique »

Seulement 2 CRA sur 3 contenaient les 4 éléments indispensables pour une analyse de base. L'atteinte ganglionnaire pN était moins souvent renseignée que tous les autres éléments rentrant en compte dans les analyses du niveau de base. Ce constat est identique à celui fait par Yesufe *et al.* en Éthiopie entre 2014 et 2016 [31]. Ce qui suggère une insuffisance de l'examen des ganglions pour une stadification correcte des malades. Cette situation pourrait s'expliquer par une insuffisance du nombre de ganglions retrouvés dans les curages axillaires. Dans notre série, 22 % des curages axillaires dont le nombre de ganglions a été renseigné dans le CRA comportaient moins de 10 ganglions. La présence d'au moins 10 ganglions dans un curage axillaire est recommandée pour que le résultat soit recevable.

Analyses de « niveau moyen » et « niveau amélioré »

Les 3 éléments d'analyse dans un contexte de moyens limités étaient tous renseignés sur seulement 26 % des CRA de type narratif et sur 86 % des CRA de type synoptique. Les analyses de niveau amélioré étaient présentes sur la totalité des CRA de type synoptique. Bien que les CRA de type synoptique ne représentent que 7 % de tous les CRA dans notre série, cette tendance suggère que l'usage d'un canevas pré-établi favorise un meilleur remplissage des CRA. Nos résultats sont similaires à ceux obtenus dans différents pays d'Afrique subsaharienne [7,12,31]. Dans les pays développés, l'usage des CRA de type synoptique a amélioré le renseignement des comptes rendus. En Australie, Austin *et al.* ont remarqué une nette augmentation de CRA conformes entre 1997 et 2004, après l'introduction des CRA synoptiques [4].

Standardisation et comptes rendus synoptiques

Les résultats de notre étude et les données de la littérature montrent que la standardisation des FDA et CRA avec usage de check-lists permet d'augmenter significativement la probabilité de communiquer des informations plus complètes ou adéquates [12]. Idowu *et al.*, dans l'étude la plus large que nous ayons trouvée, ont étudié 2125 CRA provenant de 86 établissements aux États-Unis. Les résultats montraient que 68,8 % de tous les CRA comprenaient tous les éléments requis. Ce pourcentage était nettement plus élevé dans les structures qui faisaient usage de CRA synoptiques en comparaison des structures qui faisaient usage de CRA narratifs (88 % contre 34 %) [12]. Il serait donc judicieux que les sociétés savantes, de concert avec les autorités sanitaires des pays d'Afrique subsaharienne, éditent des recommandations et instaurent l'usage de CRA de type synoptique dans les laboratoires d'anatomie pathologique. Il faudrait en outre investir dans le renforcement des capacités humaines et matérielles de ces laboratoires.

Conclusion

Un diagnostic histopathologique précis est l'un des piliers de la prise en charge du cancer du sein. Dans les pays à faibles ressources, des efforts doivent être faits pour s'assurer de la qualité des examens biologiques en général, et en particulier de la rédaction des comptes rendus d'examen anatomopathologique.

Notre étude montre que les pratiques des professionnels de santé ne sont pas toujours conformes aux recommandations disponibles. L'édition de FDA et de CRA avec items prédéfinis, validés par les sociétés savantes devrait améliorer l'exhaustivité des renseignements fournis par ces documents. Une politique de santé publique et la recherche de financements publics doivent être mises en place pour permettre une meilleure accessibilité aux moyens diagnostiques et thérapeutiques, notamment l'immunohistochimie et les thérapies ciblées qui amélioreraient les pratiques des professionnels et par conséquent, la prise en charge des patientes et leurs chances de guérison.

Considérations éthiques

Nous avons informé les différents chefs de service et les départements des affaires médicales des hôpitaux et laboratoires concernés par notre étude. Nous avons obtenu leurs autorisations et coopérations pour la collecte des données.

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Contribution des auteurs

Conception de l'étude : Freddy Houéhanou Rodrigue GNANGNON, Falilatou SEIDOU, Fèmi Perez ODIDI, Dansou Gaspard GBESSI. Collecte des données : Fèmi Perez ODIDI, Freddy Houéhanou Rodrigue GNANGNON, Falilatou SEIDOU, Christel Marie LALEYE, Arielle FLENON NAKOU.

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Liens d'intérêts

Les auteurs ne déclarent aucun lien d'intérêts.

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III.4. Épidémiologie et caractéristiques cliniques du cancer du sein à Cotonou (2014-2019) : à partir d'une étude basée sur le registre du cancer en population

Le cancer du sein se classe au premier rang mondial en termes d'incidence et de mortalité. Au Bénin, il est la première cause de décès par cancer chez la femme et représente 44,3 % de l'ensemble des cancers féminins selon une étude hospitalière publiée en 2015. A notre connaissance peu d'études ont été consacrées, au Bénin, à l'épidémiologie du cancer du sein en population générale. Ces données sont pourtant cruciales pour évaluer les progrès réalisés.

Cette étude visait à enquêter sur l'épidémiologie des cancers du sein diagnostiqués entre 2014 et 2019 chez les femmes vivant à Cotonou. Il s'agissait d'une cohorte rétrospective incluant les patientes atteintes de cancer du sein enregistrées dans la base de données du Registre du Cancer de Cotonou du 01/01/2014 au 31/12/2019. Les logiciels R 3.6.1 et SPSS ont été utilisés pour l'analyse des données. Les variables qualitatives ont été exprimées sous forme de pourcentages, et les variables quantitatives ont été décrites par des moyennes et des écarts-types. La méthode de Kaplan-Meier a été utilisée pour estimer la survie des patientes. L'incidence brute du cancer du sein variait de 16,8 cas pour 100 000 habitants en 2014 à 24,7 cas pour 100 000 habitants en 2019, avec un pic de 38,9 cas pour 100 000 habitants en 2018. L'âge moyen des sujets était de $49,6 \pm 11,9$ ans. La majorité des patientes béninoises étaient diagnostiquées aux stades III et IV. De même, la taille tumorale T4 était la plus couramment observée au moment du diagnostic, et le cancer du sein triple négatif était le sous-type moléculaire le plus répandu. La survie globale à 1 an était de 57 %, et à 5 ans de 37 %. La population étudiée atteinte de cancer du sein reste très jeune. La survie des patientes était faible comparée aux pays développés. Il est plus qu'important de donner la priorité à la prévention.

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Epidemiology and Clinical Features of Breast Cancer in Cotonou (2014-2019): Insights from a Population-Based Registry Study
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Dear Editor,

We wish to submit an original research article entitled “Epidemiology and Clinical Features of Breast Cancer in Cotonou (2014-2019): Insights from a Population-Based Registry ” for consideration by the Journal of Global Oncology.

Breast cancer is the most common cancer in women in 28 sub-Saharan African (SSA) countries. This research investigates the epidemiology of breast cancer in Cotonou, Benin, over a five-year period, providing valuable insights into incidence rates, patient demographics, and survival outcomes.

The study analyzed data from 277 patients registered in the Cotonou Cancer Registry. Our findings highlight a significant increase in breast cancer incidence. Notably, the average age of patients was 49.64 ± 11.89 years, and a majority were diagnosed at advanced stages (III and IV) with T4 tumors being predominant. The prevalence of triple-negative breast cancer as the most common molecular subtype was also observed. Survival rates were alarmingly low, with 57% at 1 year and 37% at 5 years, emphasizing the urgent need for improved preventive measures and early detection strategies.

Given the younger age of the affected population and the comparatively poor survival rates, this study underscores the critical need for enhanced public health initiatives and resource allocation towards breast cancer prevention and treatment in Benin. Our findings could inform policy makers and health practitioners in designing targeted interventions to improve breast cancer outcomes in the region.

We confirm that neither the manuscript nor any parts of its content are currently under consideration or published in another journal. All authors have approved the manuscript and agree with its submission to International Journal of Cancer.

Thank you for your consideration of this manuscript.

Sincerely,

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Epidemiology and Clinical Features of Breast Cancer in Cotonou (2014-2019): Insights from a Population-Based Registry Study

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ABSTRACT

Introduction: Breast cancer ranks first in the world while in terms of incidence and mortality respectively. The aim of this study was to investigate the epidemiology of breast cancers diagnosed between 2014 and 2019 in women living in Cotonou.

Method: This was a retrospective cohort that included 277 patients with breast cancer registered in the Cotonou Cancer Registry from 01/01/2014 to 31/12/2019. Qualitative variables were expressed as numbers and percentages, and quantitative variables were described by means and standard deviations. The Kaplan-Meier method was used to estimate patient survival. R 3.6.1. and SPSS software was used for data analysis.

Results: The crude incidence of breast cancer ranged from 16.8 cases per 100,000 population in 2014 to 24.7 cases per 100,000 population in 2019, with a peak of 38.9 cases per 100,000 population in 2018. The average age of the subjects was 49.6±11.9 years. The majority of Beninese patients are diagnosed at stages III and IV. Similarly, T4 tumor size is the most commonly observed at diagnosis, and triple-negative breast cancer is the most prevalent molecular subtype. Overall survival at 1 year was 57%, and at 5 years 37%.

Discussion/Conclusion: The study population affected by breast cancer remains very young. Patient survival was poor compared with developed countries. It is more than important to give priority to prevention.

Key words: Breast cancer, Epidemiology, Incidence, Cancer Registry, Survival, Benin.

INTRODUCTION

Breast cancer is the leading cancer among women worldwide, both in terms of incidence and mortality, with 2,308,897 new cases and over 665,684 deaths in 2022 according to the Global Cancer Observatory (Globocan 2022) [1].

The highest incidence rates are recorded in high income countries, but 67% of deaths worldwide occur in low- and middle-income countries (LMICs) like those of Sub-Saharan Africa (SSA) [2]. In fact although women in high-income countries have significantly higher incidence rates than those in low-income countries (54.1 versus 30.8 per 100,000), they have significantly lower mortality rates (11.3 versus 15.3 per 100,000) [1].

In Sub-Saharan Africa, female breast cancer rank first and was estimated to account for 27.3% (129 400 cases) of the 474 000 female cancer cases in 2020 [3]. It is also worth noting the absence of comprehensive data on the incidence and mortality of cancers in most Sub-Saharan African countries due to the lack of population-based cancer registries. This presents a significant obstacle for accurately estimating the cancer burden and implementing effective prevention policies, as well as for surveillance and monitoring as crucial components of national cancer control plans in the region.

In Benin, the government, through the Ministry of Health and under the supervision of the National Program for NCD control (PNLMNT), set up a population-based cancer registry in Cotonou in 2014[4]. In the country, breast cancer is known to be the leading cancer among women [5]. In 2013, in a hospital based survey, the overall 5-year survival rate for breast cancer patients was 43% [6]. In 2018, the median survival was 42 months with a 5-year survival of 40% in a hospital-based setting in Benin [7]. Data on the incidence and mortality of breast cancer derived from population-based studies are notably lacking in the country. This report marks an important milestone, as it reveals the results of the first six years of registration (2014-2019). The insights gleaned from this comprehensive dataset not only enrich our understanding of the disease burden but also lay the groundwork for evidence-based interventions and policy formulation aimed at combating breast cancer in our community.

METHODS AND MATERIALS

Study population

This was a retrospective, descriptive study with data collection over a 6 years period from January 1, 2014, to December 31, 2019. This study focused on female breast cancer cases registered by the Cotonou Cancer Registry (Benin). The population

covered by the Cotonou Cancer Registry is comprised of all individuals normally resident in the city of Cotonou, the economic capital of the Republic of Benin. The size of this population, for the years 2014–2019, was estimated based on the most recent population and the housing census (for the year 2013) [4]. The mean average population for the period 2014–2019 was 11 884 127 (6 037 577 women and 5 846 550 men)[8].

Collection and management of data

The Cotonou Cancer Registry follows the Standard Operating Procedures Manual of the African Cancer Registry Network (AFCRN). Cancer cases are registered, whatever the diagnostic basis (pathology, imaging, tumor markers, or clinical examination). Data collection is active in approximately 28 sources where cancer patients residing in Cotonou (the economic capital city of Benin Republic) are susceptible to be diagnosed and/or treated: 9 public health facilities, 14 private clinics, 5 pathology laboratories [4]. The Centre National Hospitalier Universitaire-Hubert Koutoukou Maga (CNHU-HKM) and the Centre Hospitalier Universitaire de la Mère et de l'Enfant Lagune (CHU-MEL), two tertiary level hospital and referral hospital at a national level for breast cancer management, are the registry's primary source of information for breast cancer patients. Appropriate data collection methods have been established for each source of information. Information on cancer cases (patient personal data, tumor details and treatment, source of information, and patient outcome (alive or deceased)) is extracted from data sources records on data collection forms. Various pieces of information are coded (using the International Classification of Diseases for Oncology (ICD-O 3) for tumor site and morphology) before being entered into a database managed by the CanReg5 software developed by the International Agency for Research on Cancer (IARC)[4].

Data quality and completeness

Data collection, quality control, and consistency are ensured by DepEdits and IARCTools, which are integrated into the CanReg5 system.

Vital status

Vital status was obtained by active methods. Clinical records were traced and the patient's vital status at the closing date recorded. Cases whose vital status could not be confirmed at the end of this procedure were called when a mobile number was registered in the registry record. When no further information could be obtained, home visits were made by the registry staff. Patients whose vital status (alive/dead) could not be ascertained by the closing date of the study were censored.

Ethics approval and consent to participate

The study was approved by the Health Sciences Research and Ethics Committee in Cotonou (Benin) (N°005 2021/UAC/CERSS/P/SG/R/SA).

Informed consent was obtained from all the participants and/or their legal guardians. The study was performed in accordance with the Declaration of Helsinki. Strict security measures were applied to ensure confidentiality. The completed forms were stored securely in a locked cabinet at the Laboratory of Epidemiology of Chronic and Neurological Diseases (LEMACEN) at the Faculty of Health Sciences. Access was restricted to authorized persons only.

Data analysis

Data analysis was performed using R and SPSS software. Qualitative variables were expressed in numbers and percentages, and quantitative variables were described by means and standard deviations. Survival was been estimated and described using the Kaplan-Meier curve. The age-standardized rates were adjusted to the World Standard Population.

RESULTS

Incidence and burden of breast cancer

Between 2014 and 2019, the Cotonou Cancer Registry recorded 541 cases of breast cancer, including 13 cases in men. Breast cancer was the most common cancer diagnosed in Cotonou in both sexes (22.5%) and the most common cancer in women (38%) (Figure 1-a, b). The crude incidence rate of breast cancer varied from 16.8 cases per 100 000 population in 2014 to 24.7 cases per 100 000 population in 2019, with a peak of 38.9 cases per 100 000 population in 2018 (Figure 1-c). The age-standardised incidence (ASR) per 100 000 population ranged from 22.8 in 2014 to 45.9 in 2019, with a peak of 59.3 in 2018 (Table 1).

Characteristics of breast cancer patients

We were able to trace the medical records of 277 female patients out of the 528 cases of female patients listed by the Cotonou Cancer Registry. Age at diagnosis ranged from 20 to 91 years, with a mean age of 49.6 ± 11.9 (Table 2). Approximately 54.16% of patients were under 50 years old at the time of diagnosis. The majority of breast cancer patients were traders (24.9%) or homemakers (19.5%). In terms of education, the highest proportion of level of education among patients was “no education” (28.8%), followed by “secondary education” (25.6%). The majority of patients lived in urban areas (88.4%) (Table 3).

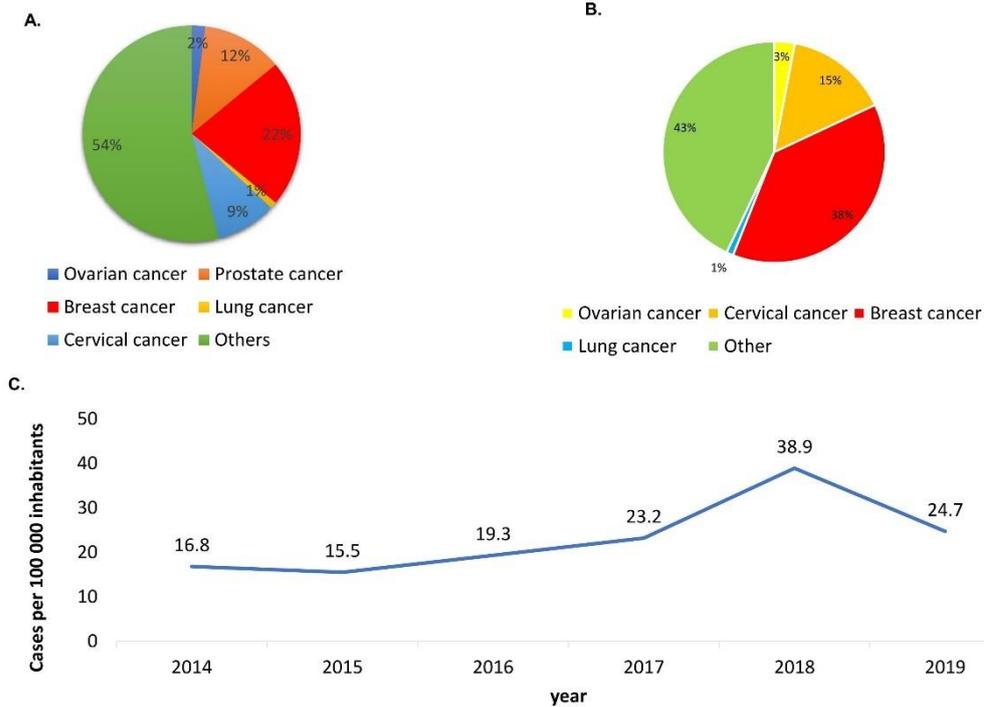


Figure 1. A) Most frequent cancers in Cotonou 2014-2019, both sexes. B) Most frequent cancers in female in Cotonou 2014-2019. C) Crude Incidence rates of breast cancer in Cotonou from 2014 to 2019)

Table 1: Crude and age-standardised incidence (100 000 inhabitants), Cotonou 2014-2019.

AGES \ YEARS	<20	<35	<45	<55	<65	<75	80+	CRUDE RATE	ASR
2014	5.4	31.7	118.1	145.3	128.3	105.3	0.0	16.8	22.8
2015	2.7	42.1	109.1	132.8	79.8	188.6	130.5	15.5	22.0
2016	0.0	65.1	127.6	132.8	145.4	182.5	0.0	19.3	26.0
2017	0.0	77.9	157	178.6	155.5	110.7	0.0	23.2	30.3
2018	0.0	73.3	280	291.2	452.6	230.9	287.4	38.9	59.3
2019	0.0	51.6	144	268.5	449.5	190.8	66.7	24.7	45.9

Table 2: Socio-demographic characteristics of Breast Cancer Patients

Characteristics (n=277)	Frequency	(%)
Age (years)		
<i>Mean ± SD: 49.64± 11.89</i>		
<30	6	(2.2)
[30-40]	40	(14.4)
[40-50]	104	(37.5)
[50-60]	68	(24.5)
≥60	59	(21.3)
Occupation		
Student	1	(0.3)
Unemployed	1	(0.3)
Housewife	54	(19.5)
Manual worker	32	(11.5)
Shopkeeper	69	(24.9)
Middle management	41	(14.8)
Senior manager	15	(5.4)
Not specified	64	(23.0)
Education level		
None	23	(8.3)
Primary	62	(22.4)
Secondary	71	(25.6)
Tertiary	41	(14.8)
Not specified	80	(28.8)
Residence area		
Urban	245	(88.4)
Rural	14	(5.1)
Not specified	18	(6.5)

Clinical and therapeutic characteristics

The rank of Scarff Bloom and Richardson (SBR), could be evaluated in 53.8% of which 4.7% of Grade I, 31.0% of Grade II and 18.1% of Grade III. Tumours were diagnosed at very advanced stages: stage could be evaluated in 75.1% of which 32.8% of stage III and 23.5% stage IV. Immunohistochemistry was reported for 144 patients. Of these 144 patients, 49 had triple negative tumours and 41 had luminal A tumours (Table 3). Targeted therapy was the least common type of treatment, followed by radiotherapy (Table 3).

Table 3: Clinical characteristics of Breast Cancer Patients

Laterality		
Right	135	(49.0)
Left	108	(37.2)
Bilateral	9	(3.2)
Not specified	25	(10.5)
TNM Classification		
T		
T0	2	(0.7)
T1	14	(5.0)
T2	48	(17.3)
T3	45	(16.2)
T4	115	(41.5)
Tx	28	(10.1)
Not specified	25	(9.0)
N		
N0	50	(18.0)
N1	93	(33.5)
N2	78	(28.1)
N3	16	(5.7)
Nx	17	(6.1)
Not specified	23	(8.3)
M		
M0	138	(49.8)
M1	66	(23.8)
Mx	48	(17.3)
Not specified	25	(9.1)

SBR		
SBR1	13	(4.7)
SBR2	86	(31.0)
SBR3	50	(18.1)
Not specified	128	(46.2)
UICC		
Stage 0	3	(1.1)
Stage I	20	(7.2)
Stage II	29	(10.5)
Stage III	91	(32.8)
Stage IV	65	(23.5)
Not specified	69	(24.9)
Molecular subtype		
Her2	17	(6.1)
Unclassifiable	3	(1.1)
Luminal A	41	(14.8)
Luminal B not Her	23	(8.3)
Luminal B non Her +	11	(3.9)
Triple negative	49	(17.7)
Not specified	133	(48.0)
Radiotherapy performed		
Yes	32	(11.5)
No	145	(52.3)
Not specified	100	(36.1)
Chemotherapy performed		
Yes	178	(64.3)
No	37	(13.4)
Not specified	62	(22.4)
Surgery		
Yes	144	(51.9)
No	61	(22.0)
Not specified	72	(25.9)
Hormone therapy performed		
Yes	4	(1.4)
No	143	(51.6)
Not specified	130	(46.9)

Overall Survival

The one-year overall survival rate stood at 57%, decreasing slightly to 54% at two years, followed by a notable decline to 44% at three years, and further to 37% at five years. The median survival period was recorded at 40.7 months.

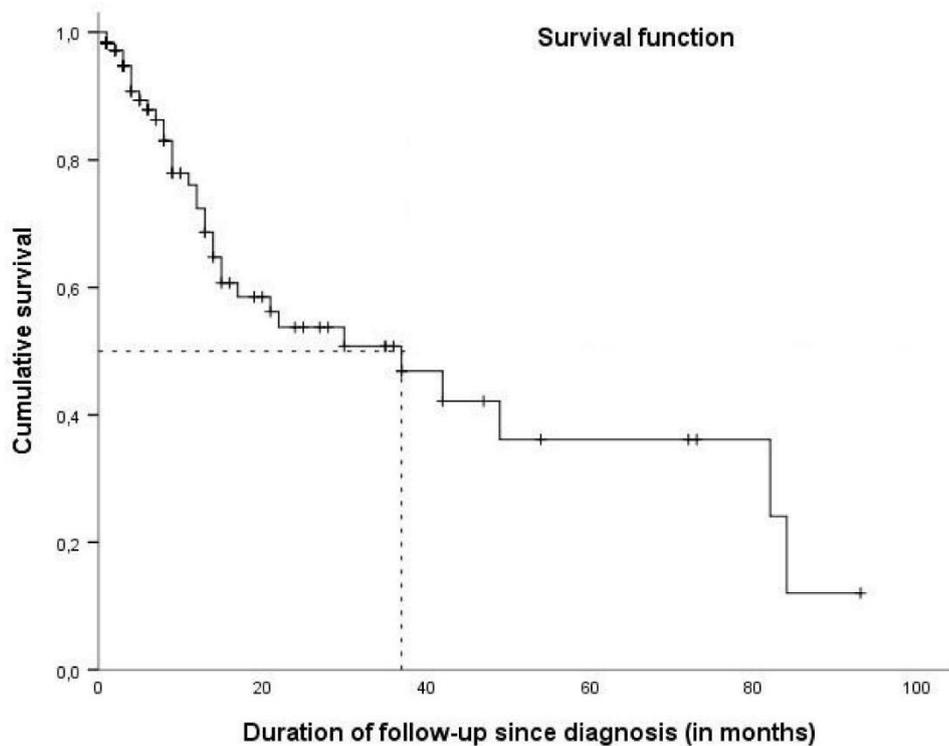


Figure-2: Overall survival of breast cancer in Cotonou between 2014 and 2019

DISCUSSION

In low- and middle-income countries (LMICs) such as Benin, where healthcare facilities are often limited or scarce, the quality of cancer registration data may be compromised [9]. However Data from the Cotonou Cancer Registry for the period 2015-2017 have been included in the 12th volume of Cancer Incidence in Five Continents [10]. Cancer Incidence in Five Continents (CI5) is a collaboration between the International Agency for Research on Cancer (IARC) and the International Association of Cancer Registries (IARC) published every five years, and is an essential source of information on the evolution of cancer incidence worldwide. The IC5 databases, which include registries whose data quality has been judged to be optimal, provide access to detailed

information on cancer incidence recorded by population-based cancer registries (sub-national or national) [11].

The crude incidence of breast cancer varied from 16.8 cases per 100,000 inhabitants in 2014 to 25 cases in 2019, with a peak of 38.9 cases in 2018. In Tunisia, Zemni et al. found a crude incidence rate of 34.25 per 100,000 inhabitants in 2022 [12]. In the study by da Silva et al (2024), the median incidence rate of breast cancer in British Columbia was 101.3 per 100,000 for white women and 59.7 per 100,000 for black women [13]. The mean age at diagnosis was 49.64 ± 11.9 years in our study. Joku Fru et al. found similar data (45.8 years) in Ethiopia in 2019 [14]. Mampionona et al. in 2021 (Madagascar) found an mean age of 52.83 years [15]. The mean age at diagnosis was 49.64 ± 11.9 years in our study. Joku Fru et al. found similar data (45.8 years) in Ethiopia in 2019 [14]. Mampionona et al. in 2021 (Madagascar) found a mean age of 52.83 years [15]. In France (2020), Dabakuyo-Yonli et al. found an average age at diagnosis of 63 years. These differences could be attributed to the relative youth of the populations and the lower life expectancy in sub-Saharan African (SSA) countries [16]. These differences could be attributed to the relative youth of populations and lower life expectancy in Sub-Saharan African (SSA) countries.

The average consultation time in this study was 8.1 months. Tonato Bagnan et al. found similar data (6 months) in 2015 in a hospital based study in Cotonou [17]. The same delay (8.1 months) was found in a study carried out in Dakar (Senegal) in 2008 [18]. However, in Tunisia, Haddad et al. in a retrospective study carried out in 2018 found an average consultation time of 5.2 months [19]. Which could reflect an effective breast cancer screening policy.

In our study, 57.7% (160 out of 277 cases) of breast cancers were diagnosed at stage T3 and T4. Similar data were found in other African series. Thus, Sando et al. found in a study conducted in Cameroon in 2014, 76.4% of cases diagnosed at stage T3 and T4 [20]. Dia et al. observed 88.6% of cases diagnosed at stage T3 or T4 in Ivory Coast (2017) [21]. In some African countries with higher socioeconomic levels, tumors are detected at earlier stages. Touria et al. in Morocco in 2016, found 12.2% (T3) and 4.1% (T4) [22]. Eric et al. in Croatia found a proportion of 8.9% for T3 and 3.8% for T4 [23]. In one of our very recently published studies (Benin 2024), tumours were most often classified as T4 (47.6%) [24]. This difference in tumor size can be explained by the fact that in countries with a high development index, cancer detection is much earlier thanks to effective awareness-raising policies. In our study, the rate of lymph node involvement was 67.3%. Sando et al. in Cameroon found 73.6% [20]. Dia et al. in Ivory Coast found a rate of 49.5% [21]. In Morocco, Touria et al. found a lymph node involvement rate of 38.9% [22]. In our study, approximately 24% of tumors were metastatic at the time of diagnosis. Joku-fru et al. found that 18.4% of tumors were metastatic at the time of diagnosis in a study conducted in 12 sub-Saharan African countries [25]. However, Sant et al, in a study conducted in several European countries (Estonia, France, Italy, the Netherlands, Spain and the UK) in 2003, showed that in both France and Italy, less than 6% (5.6-5.9%) of cases were metastatic at the time of diagnosis [26]. This indicates late diagnosis of breast cancers in our countries due to

lack of effective screening policy and available technical equipment. In our study, more than half of the patients (56%) were diagnosed at a late stage (3 and 4). Similar data were found in other African series. Tonato Bagnan et al. found in 2013 that 69.9% of breast cancers were diagnosed at a late stage (3 or 4) [17]. In a study conducted by Joko-fru et al. in 2019 on breast cancer in 12 African countries, 64.9% of cases were diagnosed at a late stage (3 or 4) [25]. In a study by Lim et al., approximately 5% of women with newly diagnosed breast cancer had stage IV at the time of diagnosis in the USA [27]. This difference is undoubtedly linked to effective screening strategies implemented in developed countries, which make it possible to detect cases of breast cancer at a very early stage.

In this study, more than one in three tumors was triple negative, followed by luminal A. These figures are similar to those found in many sub-Saharan African countries. Gnanon et al. in Benin in 2024 showed that the majority molecular type was triple negative (31.3%), followed by luminal A (25.4%)[24]. In the study by Ahuka et al. in Senegal in 2017, triple negative cancer ranks the first place in 63.6% of cases [28]. In the series by Adani-Ifè et al. in Togo, the predominant molecular subtype was also triple negative (37.6%), followed by luminal A subtype (30.8%) in 2020 [29]. In North Africa, in the study by Adjadé et al. conducted in Morocco in 2023, luminal B type was the most common (57%), followed by HER2+ (17.5%) and triple negative (16.7%)[30]. In Saudi Arabia, Al-Thoubaity et al. found in 2019 that Luminal A (58.5%) was the most common subtype, followed by triple negative (16%), Luminal B (14%) and HER2-positive (11.5%) [31]. In the United States (2022) David R. Nelson et al. showed that the most common subtype of breast cancer in their cohort was HR+, HER2- (69.6%), followed by triple-negative cancer (10.5%)[32]. This slight difference could be explained by genetic factors.

The overall survival rate for all causes combined was 57% at 1 year, 54% at 2 years, 44% at 3 years, and 37% at 5 years. Gnanon et al (Benin, 2024) found an overall survival rate of 87.61% at 1 year, 66.23% at 3 years and 48.49% at 5 years[24]. Several studies conducted in the sub-region have found slightly different data. This is the case of Joko-fru et al. in a retrospective study conducted in 2019 in 12 African countries, which found an overall survival rate at 1 year of 84.1% and 61.4% for 3-year survival [25]. In 2023, Misganaw et al. in a study conducted in Ethiopia found respective survival rates of 95% for 1-year survival, 83% for 2-year survival, 53% for 3-year survival, and 11.42% after 60 months of follow-up [33]. According to Sachon's study in 2019, in France, the 5-year survival rate was around 88%[34]. Differences in survival partly reflect variations in stage at diagnosis, tumour biology, access to high quality treatment, availability of patient data and effective awareness and early detection policies.

CONCLUSION

It appears that the incidence of breast cancer among women in Cotonou is on the rise (16.8 cases per 100,000 in 2014 to 38.9 cases per 100,000 in 2019) and affects a much younger population. Triple-negative breast cancer was the most represented type of cancer within the study population. The overall survival of women with breast cancer in Cotonou remains poorer compared to developed countries despite advances in oncology. Despite the low incidence of breast cancer in the region, compared to developed countries, we observe a higher rate of late cases due to the absence of effective screening policies, delayed access to care, deficient technical equipment, and difficulty in accessing healthcare. To improve the survival of women with breast cancer in Benin, it is important and urgent to have effective policies for screening and early diagnosis, extensive awareness campaigns, facilitate access to care, and adequately equip healthcare facilities.

LIST OF ABBREVIATIONS

CNHU-HKM : Centre National Hospitalier Universitaire Hubert KOUTOUKOU MAGA ; HER2 : Human Epidermal Growth Factor Receptor 2 ; HR : Hazard Ratio ; SBR : Scarf Bloom and Richardson ; TNM :Tumor, Node, Metastasis ; UICC : Union for International Cancer Control ; WHO : World Health Organization

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

FINANCIAL DECLARATION

This study received funding from Institute for Research on Development (IRD) to organize data collection.

AUTHORS' CONTRIBUTIONS

FHRG and AP conceived the idea for the study. FHRG, AP, HRS designed the research and analysed the data. ATE, BDY, JMM, EM and CT collected data. ATE and RBB performed statistical analyses. FHRG, AP, HRS wrote the paper. DH, PMP, VB, SA contributed to the interpretation and writing. All authors reviewed the manuscript.

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Figure 1

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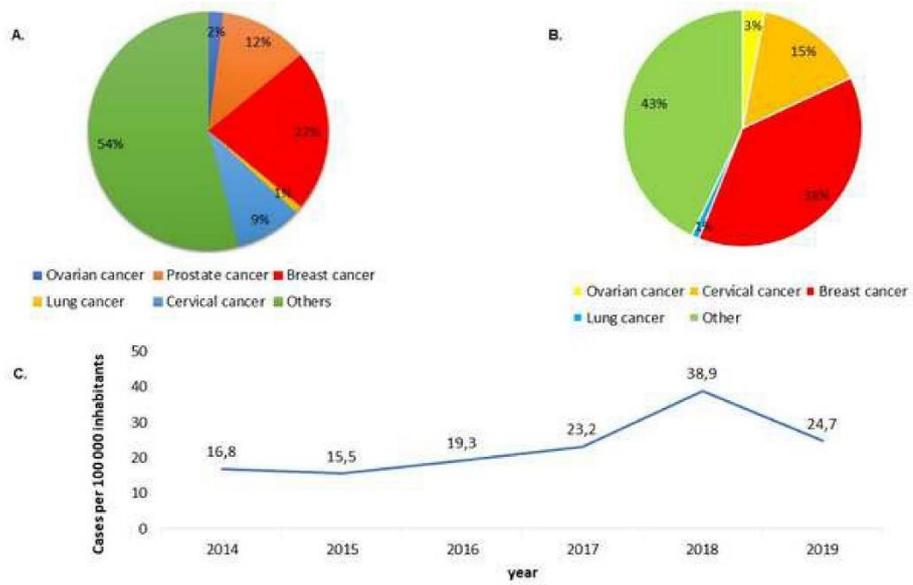
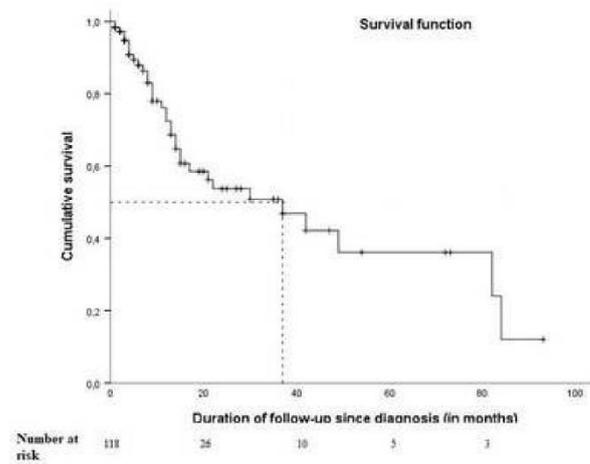


Figure 2

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III.5. Facteurs Pronostiques du cancer du sein à Cotonou

Au Bénin, pays d'Afrique de l'Ouest, le cancer du sein est le premier cancer féminin en termes d'incidence. Cependant, les données sur la mortalité du cancer du sein et ses facteurs associés manquent dans ce pays. Notre objectif était de décrire et d'analyser les aspects pronostiques du cancer du sein au Bénin.

Une étude descriptive et analytique a été réalisée au CNHU-HKM et au CHU-MEL, deux hôpitaux de référence à l'échelle nationale pour la prise en charge du cancer du sein, situés à Cotonou, la capitale économique du Bénin. Les observations médicales de patientes atteintes d'un cancer du sein avec preuve histologique et études immunohistochimiques, prises en charge dans ces deux hôpitaux de référence, entre le 1er janvier 2014 et le 30 septembre 2020, ont été rétrospectivement incluses. Nous avons analysé 319 observations médicales. L'âge moyen au moment du diagnostic était de 48,7 ans. Les tumeurs étaient le plus souvent classées T4 (47,6 %) avec un envahissement ganglionnaire N2 (34,5 %), et des métastases ont été cliniquement constatées dans 21,9 % des cas. Le stade a été rapporté dans 284 observations médicales. Les tumeurs ont été diagnostiquées à des stades (AJCC) très avancés : stade III (47,5 %) et stade IV (24,7 %). Les grades SBR 2 (49,2%) et SBR 3 (32,6%) étaient les plus fréquents. Le cancer du sein triple négatif (31,3 %) était le type moléculaire le plus fréquent. La survie globale à 5 ans était de 48,5 %. En analyse multivariée, les facteurs de mauvais pronostic étaient l'envahissement ganglionnaire (HR = 2,63 ; p = 0,026 ; CI : [1,12-6,17]), la présence de métastases (HR = 3,64 ; p < 0,001) ; CI : [2,36-5,62] et le profil immunohistochimique (HR = 1,29 ; p < 0,001) ; CI : [1,13-1,48]). Nous en avons déduit que le cancer du sein au Bénin est prédominant chez les jeunes adultes et est souvent diagnostiqué à un stade tardif. La survie des patientes atteintes d'un cancer du sein au Bénin peut être améliorée en renforçant le diagnostic précoce et la prise en charge multidisciplinaire.

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RESEARCH

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Prognostic factors and overall survival of breast cancer in Benin: a hospital-based study

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Abstract

Background In Benin, a country in West Africa, breast cancer is the leading cancer in women, both in terms of incidence and mortality. However, evidence on the mortality of breast cancer and its associated factors is lacking in this country. Our aim was to describe and analyze the clinical, histopathological, and prognostic aspects of breast cancer in Benin.

Methods A descriptive and analytical study was carried out at the CNHU-HKM and the CHU-MEL, two major tertiary referral hospitals for breast cancer management located in Cotonou, the capital city of Benin. All breast cancer medical records with histological evidence and immunohistochemistry studies were retrospectively collected between January 1, 2014, and September 30, 2020, in these two tertiary referral hospitals and analyzed in the current study.

Results Finally, 319 medical records were included. The mean age at diagnosis was 48.74 years. The tumors were most frequently classified as T4 (47.6%) with lymph node involvement N2 (34.5%), and metastases were clinically noted in 21.9% of cases. Stage was reported in the medical records of 284 patients. Tumors were diagnosed at very late AJCC stages: stage III (47.5%) and stage IV (24.7%). Grades SBR 2 (49.2%) and SBR 3 (32.6%) were the most frequent grades. Triple-negative breast cancer (31.3%) was the most common molecular type. The overall 5-year survival was 48.49%. In multivariable analysis, the poor prognostic factors were lymph node invasion (HR = 2.63; $p = 0.026$; CI: [1.12, 6.17]), the presence of metastasis (HR = 3.64; $p < 0.001$; CI: [2.36, 5.62]) and the immunohistochemical profile (HR = 1.29; $p < 0.001$; CI: [1.13, 1.48]).

Conclusions Breast cancer in Beninese is predominant in young adults and is often diagnosed at a late stage. The survival of breast cancer patients in Benin can be improved by enhancing early diagnosis and multidisciplinary management.

Keywords Breast cancer, Benin, Sub-saharan africa, Survival, Prognostic factors

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Background

With more than 2 million new cases and more than 600,000 deaths in 2020, breast cancer is the leading cancer in women worldwide, both in terms of incidence and mortality [1].

In sub-Saharan Africa, breast cancer mortality rates are among the highest, resulting particularly from late diagnosis and poor patient survival [2]. As a comparison, age-standardized mortality rates for breast cancer in 2020 were 15.5 per 100,000 in Western Europe, 8.6 per 100,000 in East Asia and 17.8 per 100,000 in West Africa [1].

Breast cancer is the most common cancer in women in 28 sub-Saharan African countries, including Benin [3]. According to the IARC (International Agency for Research on Cancer), there were 1066 new cases and 566 deaths related to breast cancer in Benin in 2020 [3]. The Beninese health system is a pyramid-type system. At the top are university hospitals, which are reference hospitals in the treatment of cancers [4]. Benin does not have hospitals specialized in cancer care. Diagnosis and treatment are financially supported by the patients themselves in most cases, although some receive assistance from the Beninese government. There is no radiotherapy equipment in Benin, and only a few oncologists are found in the country [5]. The Survcac-3 study, based on data from 68 cancer registries in 32 countries, estimated 3-year survival at over 80% in most countries. However, there were wide variations in Africa, with 3-year survival ranging from 61.7% in Zimbabwe to 87.9% in Kenya [6]. Benin was not included in the Survcac-3 study but the 3-year survival was estimated at 53% in the country [7], which is lower than the 5-year survival in Europe (84%).

Many factors can negatively affect breast cancer patient survival, including the absence of an organized screening policy, the long delay between the discovery of breast abnormalities and the necessity of treatment, late diagnosis, the obsolescence of technical facilities, and sociocultural considerations [8].

To the best of our knowledge, only a few studies have explored the clinical outcomes and prognostic factors of breast cancer in Benin [9]. In the few studies found, clinical, histological, epidemiological, and treatment data are often lacking [9].

Survival analyses constitute a powerful tool for evaluating the progress made in the management of breast cancer and are useful to monitor the impact of a cancer control plan. This study was conducted to examine the clinical, diagnostic, and prognostic aspects of breast cancer in Benin. Specifically, the following criteria were studied in combination: (i) the characteristics of patients with breast cancer, (ii) the management of breast cancer in hospitals in Cotonou, (iii) patient survival, and (iv) the factors influencing breast cancer survival in Benin.

Materials and methods

Study population

This was a retrospective, descriptive and analytical study with data collection over an 81-month period from January 1, 2014, to September 30, 2020. This study focused on female breast cancer cases managed in two hospitals in Cotonou (Benin): the Centre National Hospitalier Universitaire Hubert Koutoukou Maga (CNHU-HKM) and the Centre Hospitalier Universitaire de la Mère et de l'Enfant Lagune (CHU-MEL). These two hospitals are tertiary referral centers for the management of breast cancer at a national level in Benin. The country's population was estimated at 13.35 million in 2022, with a fertility rate of 5.7 children per woman and a life expectancy of 61.2 years [10]. Patients were included if they had (i) histologically confirmed invasive breast cancer (ii) with immunohistochemistry (estrogen receptor, progesterone receptor, HER2, Ki67) results available and (iii) were managed in the two tertiary referral hospitals during the study period. Patients were excluded from our study if they were male or had *in situ* breast cancer.

Data collection

Relevant data were collected from (i) the admission registries of the surgery, oncology and gynecology departments of the CNHU-HKM and the CHU-MEL, (ii) the patients' medical records, (iii) the registries of the operating rooms, the intensive care unit, and the hospitalization of these departments, and (iv) the family members of patients who died of breast cancer, when available. A standardized collection form was developed for the study. The form included sociodemographic data (age at diagnosis, occupation, level of education, etc.); clinical data (patients' main complaints, time between appearance of the first symptoms and date of consultation, performance status, clinical stage, etc.); paraclinical data (mammography, histology type and grade, etc.); treatment methods (surgery, chemotherapy, targeted therapy, radiotherapy, etc.). The date of the first symptoms was reported by the patient. The date of diagnosis was the date of histological confirmation of breast cancer. The threshold for defining breast cancer in young women is controversial (35 versus 40 years at the time of diagnosis). In this study, the threshold of 35 years was chosen to define breast cancer in young women [11]. The data collection tool was pretested on twenty patients. General status was estimated using the ECOG (Eastern Cooperative Oncology Group) performance status (PS) at the first medical visit after cancer diagnosis. The ECOG Performance Status also called WHO (World Health Organization) Performance Status is an assessment of the patients' actual level of function and capability of self-care [12]. Cancer cases were staged according to the UICC-TNM (Union for International Cancer Control- Tumor, Node,

Metastasis) classification and the AJCC (American Joint Committee on Cancer) classification [13] based on the data obtained from the medical records. The American College of Radiology (ACR) classification was collected from the imaging reports, and the Scarf Bloom and Richardson (SBR) histopronostic grade [14] was reported from the pathology reports. The immunohistochemical profile of tumors was determined based on anatomobiochemical findings and the evaluation of estrogen and progesterone receptors, the overexpression of HER2, and the proliferation index Ki67 [15]. The disease outcome included three modalities: death, survival and loss to follow-up. The medical records were reviewed, and telephone interviews were conducted with patients or their family members when they were lost to follow-up to determine the disease outcome when possible. When necessary, home visits were made to actively assess the patients' condition. The cutoff date was September 30, 2020.

Table 1 Socio-demographic characteristics of breast cancer patients

Characteristics (n=319)	Frequency	(%)
Age (years)		
<i>Mean ± SD: 48.74 ± 11.73</i>		
<30	6	(1.88)
[30–40]	62	(19.44)
[40–50]	116	(36.36)
[50–60]	72	(22.57)
[60–70]	48	(15.05)
[70–80]	12	(3.76)
≥ 80	3	(0.94)
Occupation		
Student	2	(0.6)
Unemployed	1	(0.3)
Housewife	87	(27.3)
Manual worker	46	(14.4)
Shopkeeper	65	(20.4)
Middle management	44	(13.8)
Senior manager	15	(4.7)
Not specified	45	(14.1)
Other	14	(4.4)
Education level		
None	60	(18.8)
Primary	78	(24.5)
Secondary	89	(27.9)
Tertiary	51	(16.0)
Not specified	41	(12.9)
Residence area		
Urban	246	(77.1)
Peri-urban	27	(8.5)
Rural	8	(2.5)
Not specified	38	(11.9)

Data analysis

Data collected were recorded using Epi Data 3.1 software, and data analysis was carried out using STATA version 15 software. Qualitative variables were expressed as numbers and percentages, and quantitative variables were described by means and standard deviations.

Overall survival was analyzed by the Kaplan–Meier method, and the log-rank test was used for the comparison of survival rates between groups. To determine the factors associated with survival, a Cox regression analysis was performed. The proportional hazards assumption was tested for each variable in the Cox model, and the associated coefficient was stable over time. A p value < 0.05 was considered statistically significant.

Results

Characteristics of breast cancer patients in Benin

A total of 677 patients with breast cancer were registered in both hospitals from 2014 to 2020. Of these, 324 patients (47.9%) received immunohistochemistry. Male cancer patients (3 men) and 2 patients with in situ cancer were excluded from the study sample. In total, 319 patients were included in our study. The age at diagnosis ranged from 19 to 85 years, and the mean age was 48.74 ± 11.73 (Table 1). Approximately 57.68% of the patients were under 50 years old at the time of diagnosis. The majority of breast cancer patients were housewives (27.3%) or shopkeepers (20.4%). In terms of education, patients' highest level of education was secondary school (27.9%), a primary school level (24.5%), a tertiary school level (16%) or no education (18.8%). Finally, the majority of patients lived in urban areas (77.1%) (Table 1).

Of the 319 breast cancer cases included in our study, the majority had no previous known personal history of benign breast disease (95.3%). Many patients had 4 or more pregnancies (45.7%), of whom 218 had practiced breastfeeding. Up to 87.1% of patients had never used oral contraception. Out of 319 patients, 43 had a family history of breast cancer, and 3 had a family history of ovarian cancer (Table 2).

The main reason for consultation was an "incidental discovery of a breast nodule by the patient" in 92.2% of cases. The time between the onset of symptoms and the first consultation was more than 6 months for 31.6% of patients. The majority of patients (76.8%) had a good general condition (according to ECOG Performance Status) at the time of diagnosis. Regarding laterality, 51.1% of breast tumors were located in the right breast, 41.4% were located in the left breast, and 0.3% were bilateral.

Regarding the tumor size/stage, most cases were classified as T4 (47.6%) at the time of diagnosis. For lymph node status, the majority of patients were classified as N2 (34.5%) or N1 (32.3%). Seventy patients (21.9%) had metastases at the time of diagnosis, mainly in the lung

(53.6%) or bone (39.1%) (Table 2). Stage (AJCC-American Joint Committee on Cancer) was reported in the medical records of 284 patients. More than 70% of patients were diagnosed at a late stage. Specifically, tumors were classified as AJCC stage III (47.5%), stage IV (24.7%), stage II (21.8%) and stage I (6.0%) at diagnosis (Fig. 1A).

More than half of the patients underwent mammography (59.6%) and ultrasound (66.5%) for diagnostic purposes. Tumors were classified as ACR4 (American College of Radiology) in most cases (22.3%). The most common histological type was non-specific carcinoma ($n=305$, 95.6%), followed by lobular carcinoma ($n=9$, 2.8%) and mucinous carcinoma ($n=5$, 1.6%). Regarding the histopronostic grade (Scarff-Bloom-Richardson grading system), SBR grade II (49.2%) and SBR grade III (32.6%) were the most predominant in our study (Table 2).

The breast cancer molecular subtypes were distributed as follows: triple negative (31.3%), luminal A (25.4%), luminal B Her2- (21.6%), luminal B Her2+ (11%) and Her2 (10.7%) (Fig. 1B).

Survival of breast cancer patients in Benin

Overall survival was 87.61%, 66.23% and 48.49% at years 1, 3, and 5, respectively (Fig. 2A). The 5-year overall survival of patients was significantly lower when the time between the onset of symptoms and the first consultation was higher than 6 months ($p=0.0008$) (Fig. 2B). Patients diagnosed before the age of 35 were more frequently found to have a poor 5-year overall survival (40.34%) than patients diagnosed after the age of 35 (48.84%) (Fig. 2C), but the difference was not statistically significant ($p>0.05$).

In particular, the 5-year overall survival of patients decreased with increasing primary tumor size ($p<0.001$) with T1 (91.76%), T2 (73.43%), T3 (55.19%) and T4 (34.37%) (Fig. 3A). Patient 5-year survival was also associated with clinical lymph node involvement. Patients with clinical lymph node involvement (N+) had a lower probability of survival (42.69%) than those without lymph node involvement (N0) (74.29%) ($p=0.0002$) (Fig. 3B). Similarly, patients with metastases (M1) had poorer 5-year survival than those without metastases (M0) (6% vs. 63.95%), and this difference was statistically significant (Fig. 3C). Patient survival was also associated with histopathologic grade (Scarff-Bloom-Richardson grading system). The 5-year survival was 36.53% for grade 3 tumors (SBR3), 48.94% for grade 2 tumors (SBR2) and 67.15% for grade 1 tumors (SBR1). The difference was statistically significant ($p=0.0045$) (Fig. 3D).

Considering the AJCC (AJCC 7th anatomic staging system), the 5-year overall survival decreased significantly ($p<0.001$) with each stage: stage I (94.12%), stage II (79.65%), stage III (54.44%) and stage IV (6%) (Fig. 4A).

Finally, the immunohistochemical profile of the tumors also influenced the prognosis of the patients. Indeed, triple-negative breast cancer had a poor 5-year survival (33.19%) compared to luminal A (54.89%), luminal B Her2- (53.17%), luminal B Her2+ (68.89%) and Her2 (48.95%) ($p=0.0001$) (Fig. 4B).

After multivariable analysis, the prognostic factors were as follows (Table 3): lymph node invasion (HR=2.63; $p=0.026$, CI: [1.12, 6.17]), presence of metastasis (HR=3.64; $p<0.001$; CI: [2.36, 5.62]) and triple-negative immunohistochemical profile (HR=1.29; $p<0.001$; CI: [1.13, 1.48]).

Discussion

This retrospective study conducted from January 1, 2014, to September 30, 2020, included patients treated for breast cancer in two tertiary referral hospitals in Benin (West Africa) who had benefited from immunohistochemistry for molecular profiling. The sociodemographic characteristics of the patients and the clinical, anatomical, and immunohistochemical characteristics of the tumors were determined. Patient survival and the prognostic factors of breast cancer were analyzed.

The mean age of diagnosis of breast cancer in our study was 48.74 ± 11.73 years. The data are comparable to those of other African countries, 45.0 years in Mali and 46.8 years in Cameroon [16, 17]. The average age at diagnosis is therefore much lower than in developed countries such as France, which is approximately 63 years [18, 19]. This young age of breast cancer occurrence in SSA may be more a reflection of the structure of the African populations (very young with a broad-based age pyramid) than a real susceptibility. More generally, according to Hemminki et al [20], the low age of diagnosis of breast cancer in developing countries such as those of SSA can be explained by 3 factors.

- The first line refers mainly to biological differences; for example, studies carried out in the Caribbean suggest that one black or afro-descendant woman in 7 has genetic breast cancer [21].
- The second refers to a cohort effect in relation to the high proportion of young subjects in the populations of these countries.
- The third refers to the incomplete registration of cancer in older people who may have poorer access to cancer care in developing countries.

Beninese patients were housewives and had no or low levels of education in most cases. In European and American studies, high socioeconomic status is considered a risk factor for breast cancer. In France, Orsini et al. noted a predominance of high socioeconomic status (65%) among women diagnosed with breast cancer [22].

Table 2 Clinical characteristics of breast cancer patients

Characteristics (n = 319)	Frequency	(%)
History of benign breast disease		
Yes	15	(4.7)
No	304	(95.3)
Number of pregnancies		
0	14	(4.4)
1	27	(8.5)
2–3	93	(29.2)
4 and more	146	(45.7)
Not specified	39	(12.2)
Number of children		
0	22	(6.9)
1	44	(13.8)
2–3	116	(36.4)
4 and more	98	(30.7)
Not specified	49	(12.2)
Breastfeeding		
Yes	218	(68.4)
No	101	(31.6)
Hormonal oral contraception		
Yes	41	(12.9)
No	278	(87.1)
Family history of breast cancer		
Yes	43	(13.5)
No	276	(86.5)
Family history of ovarian cancer		
Yes	3	(0.9)
No	316	(99.1)
Reasons for consultation		
"orange peel" appearance of the breast.	16	(5.0)
Nodule	294	(92.2)
Mastodynia	22	(6.9)
Nipple discharge	7	(2.2)
Skin ulceration	10	(3.1)
Revealing metastasis	3	(0.9)
Axillary adenopathy	5	(1.6)
Consultation time		
< 6 months	168	(52.7)
≥ 6 months	101	(31.6)
Not specified	50	(15.7)
Patient general condition at diagnosis (ECOG PS)		
0	245	(76.8)
1	22	(6.9)
2	5	(1.6)
3	6	(1.9)
4	3	(0.9)
Not specified	38	(11.9)
Laterality		
Right	163	(51.1)
Left	132	(41.4)
Right and left	1	(0.3)
Not specified	23	(7.2)

Table 2 (continued)

Characteristics (n = 319)	Frequency	(%)
TNM Classification		
T		
T1	12	(3.8)
T2	67	(21.0)
T3	57	(17.9)
T4	152	(47.6)
Tx	31	(9.7)
N		
N0	62	(19.4)
N1	103	(32.3)
N2	110	(34.5)
N3	12	(3.8)
Nx	32	(10.0)
M		
M0	212	(66.2)
M1	70	(21.6)
Mx	37	(12.2)
Metastasis location		
Brain	7	(8.7)
Lung	37	(53.6)
Liver	26	(37.7)
Bone	27	(39.1)
Pleura	2	(2.9)
Spleen	1	(1.4)
Distant lymph node	1	(1.4)
Mammography performed		
No	129	(40.4)
Yes	190	(59.6)
ACR mammography classification		
ACR 0	14	(4.4)
ACR 1	2	(0.6)
ACR 2	4	(1.3)
ACR 3	34	(10.7)
ACR 4	71	(22.3)
ACR 5	29	(9.1)
Not specified	165	(51.7)
Ultrasound scan performed		
No	107	(33.5)
Yes	212	(66.5)
SBR		
SBR1	39	(12.2)
SBR2	157	(49.2)
SBR3	104	(32.6)
Not specified	19	(6.0)
Radiotherapy performed		
Yes	61	(19.1)
No	135	(42.3)
Not specified	123	(38.6)
Chemotherapy performed		
Yes	260	(81.5)
No	59	(18.5)
Endocrine therapy performed		
Yes	69	(21.6)
No	49	(15.4)
Not specified	201	(63.0)

Table 2 (continued)

Characteristics (n = 319)	Frequency	(%)
Targeted therapy performed		
Yes	12	(3.8)
No	30	(9.4)
Not specified	277	(86.8)

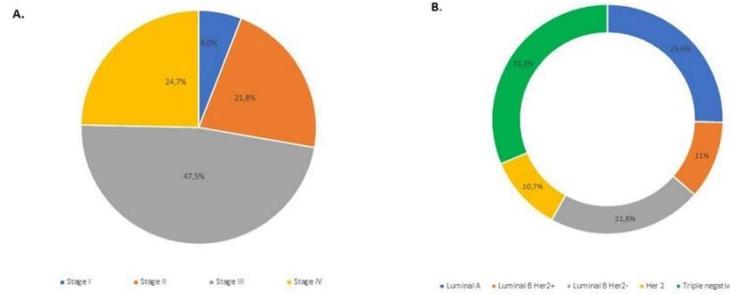


Fig. 1 Characteristics of Beninese breast cancer patients by stage at diagnosis and molecular subtype. **(A)** Distribution of breast cancer cases by stage (AJCC Stage I to Stage IV) at diagnosis (n = 284). **(B)** Distribution of breast cancer cases by molecular subtype (Luminal A, Luminal B Her2+, Luminal B Her2-, Her2 or triple negative) (n = 319)

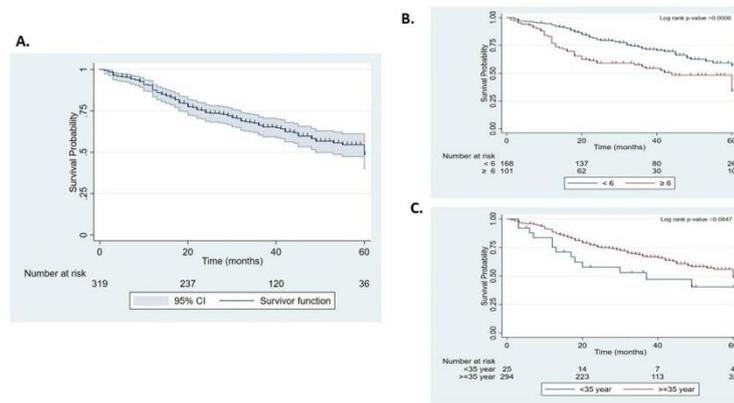


Fig. 2 Kaplan–Meier survival curves for Beninese breast cancer patients. **(A)** Overall survival curves of patients. **(B)** Overall survival curves of patients according to the time between the onset of symptoms and the first consultation (approximately 6 months). **(C)** Overall survival curves of patients according to the age of the patient at the time of diagnosis (approximately 35 years old)

Similarly, in the USA, Lehrer et al. found an association between the occurrence of breast cancer and a high socioeconomic level of patients [23]. These women have a lifestyle that promotes the accumulation of risk factors, i.e., the absence of breastfeeding, easy access to oestrogenic hormonal contraception and late first pregnancy, among others [23, 24]. The Westernization of lifestyles currently observed in SSA could contribute to the projected increase in the incidence of breast cancer in the coming decades. Patients in our study had a family

history of breast cancer in 13.5% of cases. Several studies have shown that the relative risk of a family history of breast cancer is 1.9 for any form of relationship. This risk is higher in younger women and when the disease develops in a first-degree relative before the age of 50 [25, 26].

Although it is estimated that 50% of Benin's population will live in rural areas [27], only 2.5% of breast cancer patients treated in the two national referral hospitals lived in rural areas. This finding may reflect the poor access to cancer care for rural populations in the country. Geographical

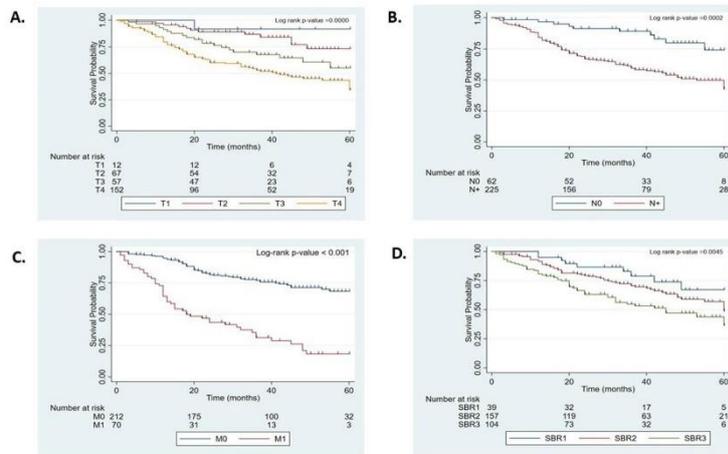


Fig. 3 Kaplan–Meier survival curves for Beninese breast cancer patients with different characteristics. **(A)** Overall survival curves of patients according to tumor stage at diagnosis (T1 to T4). **(B)** Overall survival curves of patients according to lymph node involvement at diagnosis (patients with lymph node involvement (N+) or without lymph node involvement (N0)). **(C)** Overall survival curves of patients according to metastases at diagnosis (patients with metastases (M1) or without metastases (M0)). **(D)** Overall survival curves for patients according to the histopronostic grade of the tumor at diagnosis (grade 1 tumors (SBR1), grade 2 tumors (SBR2) or grade 3 tumors (SBR3)). The log-rank test showed significant differences in survival among groups in the four panels (all $P < 0.01$)

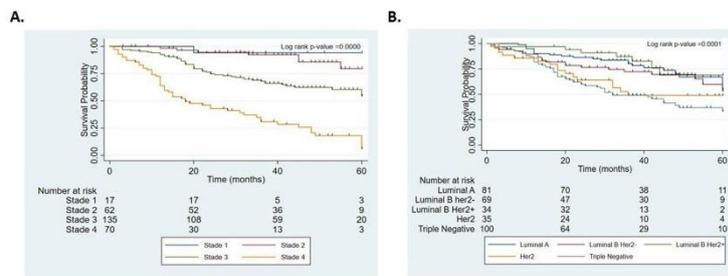


Fig. 4 Kaplan–Meier survival curves for Beninese breast cancer patients at different stages at diagnosis or of different molecular subtypes. **(A)** Overall survival curves of patients according to stage at diagnosis (Stage I to Stage IV). **(B)** Overall survival curves of patients according to molecular subtype. The log-rank test showed significant differences in survival among groups in the two panels (all $P < 0.01$)

Table 3 Multivariate analysis of factors associated with survival of cotonou breast cancer patients from 2014 to 2020

Variable	HR	p-value	[95% Conf Interval]
Consultation time	1.232	0.333	0.808 1.877
Nodes	2.63	0.026	1.122 6.167
Metastases	3.641	< 0.001	2.358 5.623
Immunohistochemical profile	1.292	< 0.001	1.129 1.48
SBR Class	1.125	0.516	0.788 1.608

remoteness, limited resources, lack of access to innovative therapies and reduced availability of interdisciplinary treatments are among the major obstacles to access to cancer care for rural populations around the world [28]. In low- and middle-income SSA countries such as Benin, these challenges are disproportionately exacerbated [28].

As in most developing countries [29], the most frequent reason for consultation in our study was the patient’s self-discovery of a breast mass, in 92.2% of cases. In developed countries, the implementation of organized screening policies has made it possible to diagnose tumors at an infra-clinical stage [30, 31]. The lack of screening, the low socioeconomic status of patients, sociocultural

considerations (breast cancer and its treatment are still taboo or stigmatizing in some communities) and the frequent use of traditional medicine as a first line of treatment explain the delayed consultation times observed in our study and in other sub-Saharan African countries [29].

In our series, the breast tumors were advanced at the time of diagnosis, with a T4 tumor rate of 47.6%. This is consistent with what is observed in other Sub-Saharan countries, such as Côte d'Ivoire and Republic of Congo [32]. A larger tumor size is associated with a higher risk of lymph node involvement and metastasis. In our study, lymph node involvement was very frequent at diagnosis. The presence of metastases varies according to the level of care in each country. Metastasis rates are generally high in developing countries, 21.9% in our study and 29.3% in Morocco [33], compared to developed countries, where the frequency varies from 5.0 to 9.4% [34, 35]. According to the AJCC staging system, the tumors were classified as stage III and IV at diagnosis in more than 70% of cases, a finding that is consistent with data from other countries in sub-Saharan Africa [16, 32, 36]. These findings are a reminder that it is crucial, particularly in SSA countries such as Benin, to focus on and invest massively in early detection programs, including awareness-raising, if we are to hope to reverse the trend towards late diagnosis and consequently reduce mortality. Intermediate grade (SBR2) and high grade (SBR3) tumors were the most frequent in our study at rates of 49.2% and 32.6%, similar to rates in several other studies in Africa [34, 37]. Breast cancer is not a single disease, because there are several subtypes, each characterized by different biological behavior; black and afro-descendant women seem to develop the most aggressive profiles [38].

Our study showed a very high prevalence of triple-negative breast cancers (31.3%) in contrast with other regions of the world, especially in white populations ($\leq 10\%$ triple-negative tumors; 66% luminal A) [39]. This high prevalence of this aggressive triple-negative type is also the most frequent in Africa, for example, 58.3% in Ghana [40]. These triple-negative tumors are often found in young women and are thought to be associated with genetic changes, particularly the BRCA 1 mutation [41–43]. These different histopronostic elements constitute factors of disease severity and other predictive factors of response to treatment.

Radiotherapy required for breast cancer management was performed in 19.1% of cases in our study. This proportion is low compared to the high number of locally advanced tumors and is explained by the absence of radiotherapy services in our country to date. The patients who benefited from radiotherapy were those who were evacuated abroad for the global management of breast cancer. The establishment of a radiotherapy service would favor access to radiotherapy and reduce the number of

medical evacuations outside Benin [44]. Hormone therapy was used in 21.6% of patients. It was indicated in 118 patients in our study (36.8%).

The high cost of the molecule and the absence of a state subsidy explain the low accessibility of targeted therapy in our study. Apart from a subsidy, this therapy is not accessible to the majority of patients because they have a low socioeconomic level.

In our study, the 3-year and 5-year survival rates of patients were 66.23% and 48.49%, respectively. In 2013, the 5-year survival for breast cancer was 43% in a single hospital in Cotonou [45]. Therefore, it seems that breast cancer survival is improving. A study of the African Cancer Registry Network in 14 African countries, including Benin, estimated 3-year survival at 19.3% in Zimbabwe, 44.1% in Mali and 49.5% in Kenya [7]. These results indicate poor survival in Africa in contrast to developed countries such as France, where the 5-year survival was 78.2% [34], and England, where it was 80.9% [46].

The Global Breast Cancer Initiative (GBCI), led by WHO recommends that policies to reduce breast cancer mortality should focus on three pillars: (i) promoting health and early detection by detecting at least 60% of cases in the early stages (I or II); (ii) improving prompt access to diagnosis and treatment, in particular by providing a diagnosis within 60 days of the first contact with the first healthcare professional; (iii) comprehensive treatment and supportive care in particular by ensuring comprehensive multimodal treatment for 80% of patients [47].

Our study was limited by the high rate of breast cancer patients with unavailable IHC results. This is a retrospective, descriptive and analytical study on patients managed for histologically confirmed breast cancer with immunohistochemical characterization. Retrospective studies conducted in developing countries such as Benin are sometimes made difficult by the nonexistence of computerized patient records. Physically archived records are often difficult to retrieve or unusable.

However, our study was conducted in two national reference centers for the management of breast cancer in Benin. This multicentric character and the sample size obtained by an exhaustive survey of cases was sufficient to allow an evaluation of the prognostic factors of breast cancers in Benin.

Conclusion

The survival of breast cancer patients seems to have improved in our country, but it remains poor compared to developed countries, given the characteristics of the patients, the stage of the disease, the molecular profile of the tumor and the inadequacy of the technical platform. To improve patient survival, it is important to implement a policy of mass screening for breast cancer allowing early detection of breast masses and to ensure

multidisciplinary management through the availability of most diagnostic and therapeutic means. These resources, combined with early detection policies, which have been absent from breast cancer care in Cotonou until now, will also improve patients' involvement in treatment and their quality of life.

Abbreviations

ACR	American College of Radiology
AJCC	American Joint Commission on Cancer
CNHU-HKM	Centre National Hospitalier Universitaire Hubert KOUTOUKOU MAGA
CHU-MEL	Centre Hospitalier Universitaire de la Mère et de l'Enfant Lagune
ECOG	Eastern Cooperative Oncology Group
HER2	Human Epidermal Growth Factor Receptor 2
HR	Hazard Ratio
IARC	International Agency for Research on Cancer
KI-67	Proliferation index
SBR	Scarff Bloom and Richardson
SSA	Sub-Saharan Africa
TNM	Tumor, Node, Metastasis
UICC	Union for International Cancer Control
USA	United States of America
WHO	World Health Organization

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Author contributions

PMP, DJL and HDS conceived the idea for the study. GFHR, PA, AM, and K-M Y designed the research and analyzed the data. GFHR, PA and K-M Y collected data. GFHR, PA and TT performed statistical analyses. GFHR and PA wrote the paper. GDG, TBJA, LA, PMP, DJL, and BV contributed to the interpretation and writing. All authors reviewed the manuscript.

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Data availability

Data for this study contain confidential patient information. The data sets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Health Sciences Research and Ethics Committee in Cotonou (Benin) (N°017-2021/UAC/CERSS/P/SG/R/SA). Informed consent was obtained from all the participants and/or their legal guardians. The study was performed in accordance with the Declaration of Helsinki. Strict security measures were applied to ensure confidentiality. The completed forms were stored securely in a locked cabinet at the Laboratory of Epidemiology of Chronic and Neurological Diseases (LEMACEN) at the Faculty of Health Sciences. Access was restricted to authorized persons only.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Chapitre IV. DISCUSSION GENERALE

IV.1. Synthèse des résultats

Cette thèse a non seulement permis de décrire le fardeau du cancer du sein au Bénin mais également de préciser des éléments de l'épidémiologie analytique (facteurs pronostiques) et de la capacité du système de santé à prendre en charge cette maladie en ASS. De plus, elle a permis de mettre en évidence, des difficultés de coordination et de communication entre les médecins intervenant dans la prise en charge des patients atteints d'un cancer du sein.

Le cancer du sein au Bénin, est le cancer le plus fréquent chez la femme représentant 38% des cancers de la femme selon les données du registre des cancers de Cotonou. Son incidence brute a varié de 16,8 cas pour 100 000 habitants en 2014 à 24,7 cas pour 100 000 habitants en 2019. L'âge moyen au moment du diagnostic était de 48,7 ans. Il était souvent diagnostiqué à un stade tardif. Les tumeurs étaient le plus souvent classées T4 (47,6 %) avec un envahissement ganglionnaire N2 (34,5 %), et des métastases ont été cliniquement observées dans 21,6 % des cas. Les tumeurs ont été diagnostiquées à des stades AJCC (III et IV) avancés dans 64,2 % des cas. Les grades SBR 2 (49,2%) et SBR 3 (32,6%) étaient les plus fréquents. Le cancer du sein triple négatif (31,3 %) était le type moléculaire le plus fréquent. En analyse multivariée, les facteurs de mauvais pronostic étaient l'envahissement ganglionnaire (HR = 2,63 ; p=0,026 ; CI : [1,12, 6,17]), la présence de métastases (HR=3,64 ; p<0,001) ; CI : [2,36, 5,62] et le profil immunohistochimique (HR=1,29 ; p<0,001 ; CI : [1,13, 1,48]). La survie globale à 5 ans était de 48,5 %.

Cette surmortalité est en partie due à la faible capacité des hôpitaux d'ASS à assurer le continuum de la prise en charge du cancer du sein. Ainsi selon notre étude, un tiers des hôpitaux (36,2%) assurant la prise en charge chirurgicale du cancer du sein couvrait une population supérieure à deux millions d'habitants. L'échographie était disponible dans tous les hôpitaux ; cependant, elle n'était pas systématiquement fonctionnelle dans 23,4 % des cas. Seule la moitié des hôpitaux (55,3 %) disposaient d'un anatomo-pathologiste à temps plein, tandis que les RCP (réunion de concertation pluridisciplinaire) n'étaient pas pratiquées dans 42,4 % des hôpitaux. L'équipement pour la radiothérapie n'était disponible que dans 19,1 % des hôpitaux. La moitié des hôpitaux (53,1%) disposaient de médicaments de chimiothérapie sur place. Dans deux hôpitaux sur dix (19,1%), les patients devaient parcourir plus de 50 kilomètres pour accéder aux médicaments de chimiothérapie.

Au-delà des capacités du système de santé à assurer le continuum des soins, les difficultés de coordination entre les médecins sont parfois source de retard diagnostique, d'erreurs médicales et de décès. Dans cette thèse, nous avons également évalué la complétude des formulaires de demande et des comptes rendus d'examen anatomopathologique de pièces opératoires de cancers

du sein chez les femmes au Sud du Bénin. Les formulaires de demande étaient conformes aux recommandations dans 31,3% des cas. Les comptes rendus étaient narratifs dans 92,7 % des cas et 68,8 % comportaient les critères minimaux. Nous avons donc conclu que les chirurgiens et les anatomopathologistes impliqués dans la prise en charge des cancers du sein au Bénin ne rédigeaient pas toujours entièrement les formulaires de demande et les comptes rendus d'examen anatomopathologique. Il est donc indispensable d'optimiser la coordination entre les différents acteurs de la prise en charge du cancer du sein. Cette tâche semble difficile au vu du nombre réduit de pathologistes, de chirurgiens et d'oncologues dont dispose le pays, un peu à l'image de toute l'ASS. Ce constat est encore plus frappant dans les zones rurales du continent qui constituent de véritables déserts médicaux où vivent les populations les plus précaires, qui ont un accès limité aux programmes de dépistage et sont diagnostiquées à des stades plus tardifs. Il nous semble donc indispensable de mettre en place une solution technologique pouvant permettre d'améliorer la coordination en vue d'une meilleure prise en charge des patientes.

IV.2. Méthodologie et validité des résultats

Plusieurs indicateurs permettent d'évaluer la charge du cancer dont l'incidence, la prévalence, la mortalité et les analyses de survie, les DALY (années de vie ajustées en fonction de l'incapacité), la qualité de vie, les coûts économiques, l'impact social et psychologique. L'évaluation complète du fardeau du cancer du sein est par conséquent, une tâche complexe qui nécessite la prise en compte de nombreux facteurs et l'utilisation conjointe de plusieurs méthodes ; chaque indicateur ayant ses avantages mais également ses limites. L'incidence a l'avantage de renseigner sur la dynamique d'une affection chronique comme le cancer tandis-que la prévalence est plus indiquée pour étudier la charge (Adoukonou, 2021). Ces indicateurs reposent essentiellement sur les registres du cancer populationnels. Cette estimation, dans les pays en voie de développement comme ceux d'ASS est difficile ; le nombre réduit et la fiabilité des registres des cancers de ces pays étant le plus souvent mise en cause.

Les données du registre des cancers de Cotonou pour la période 2015-2017 ont été prises en compte dans le 12^{ème} volume de Cancer Incidence in Five Continents. Cancer Incidence in Five Continents (CI5) est une collaboration entre le Centre international de recherche sur le cancer (CIRC) et l'Association internationale des registres du cancer (IARC) publiée tous les cinq ans, et est une source essentielle d'informations sur l'évolution de l'incidence du cancer dans le monde. Les bases de données de CI5 qui incluent des registres dont la qualité des données a été jugée optimale

permettent d'accéder à des informations détaillées sur l'incidence du cancer enregistrée par les registres du cancer basés sur la population (infranationaux ou nationaux) (Centre International de Recherche sur le Cancer & Association internationale des registres du Cancer, 2024). Les données du Registre des Cancers de Cotonou nous ont permis d'estimer l'incidence du cancer du sein et de déterminer sa place dans le fardeau du cancer à Cotonou pour la période 2014-2019, à travers la quatrième étude. Toutefois, le Registre des Cancers de Cotonou, à l'instar de la plupart des registres du cancer en Afrique subsaharienne, a connu une perturbation de ses activités à partir de 2020 en raison de la crise sanitaire mondiale liée à la COVID-19. Par conséquent, nous n'avons pas pu exploiter les données de cette période.

En ASS, les données sur l'incidence et la mortalité font cruellement défaut. Il est pourtant urgent de mener des travaux de qualité sur l'incidence et la mortalité du cancer du sein en ASS, pour guider des stratégies efficaces de lutte contre le cancer du sein dans ces pays. La première étude (revue systématique et méta-analyse) contribue à combler ce vide en synthétisant les principaux facteurs pronostiques du cancer du sein à l'échelle de l'Afrique subsaharienne, tout en permettant une estimation de la survie globale. Toutefois, une des limites de cette étude est qu'elle n'a pas permis d'étudier certains facteurs pronostiques pourtant intéressants, comme l'infection par le VIH-SIDA, l'indice de masse corporelle ou l'accès aux services de santé.

Une des limites importantes de la cinquième étude est liée à son caractère rétrospectif qui pourrait être à l'origine de biais. Ce recueil rétrospectif des données n'a pas permis d'évaluer avec précision tous les potentiels facteurs associés (par exemple la quantification précise de la consommation d'alcool et de tabac). De plus cette étude réalisée dans les hôpitaux de référence de la capitale du pays, pourrait ne pas être le reflet de la situation dans les autres régions du pays notamment les zones rurales où les patients ont un accès plus limité aux services de santé. Enfin, Ainsi, il convient de rappeler que plusieurs caractéristiques pronostiques importantes pour la compréhension de la survie des patients n'étaient pas disponibles dans les observations médicales (par exemple la séropositivité au VIH –SIDA).

Cependant, à notre connaissance, cette étude représente la première analyse des caractéristiques épidémiologiques et cliniques du cancer du sein au Bénin, combinée à une évaluation approfondie du profil moléculaire (elle confirme le cancer du sein triple négatif comme type dominant au Bénin), de la survie globale, et des facteurs pronostiques. Cette approche novatrice offre un aperçu panoramique de la maladie dans notre contexte, fournissant ainsi une base solide pour orienter les futures stratégies de prévention, de diagnostic et de traitement.

La deuxième étude nous a permis d'évaluer la capacité des hôpitaux d'ASS à assurer le diagnostic et la prise en charge adjuvante du cancer du sein. Les données dans ce domaine, dans la littérature africaine, sont particulièrement rares. Toutefois, cette étude connaît également des limites. D'abord elle n'a évalué que la capacité des hôpitaux assurant la prise en charge chirurgicale des cancers du sein et n'est donc peut-être pas le reflet fidèle de la capacité de tous les hôpitaux d'ASS. Par ailleurs, elle n'a pas inclus tous les pays d'ASS.

Cependant, ce travail a fourni des estimations de la disponibilité et de la qualité du traitement du cancer du sein qui, à notre connaissance, ont été peu évaluées auparavant en Afrique subsaharienne. Notre étude génère des estimations basées sur des données collectées sur le terrain, offrant ainsi une perspective inédite sur la gestion du cancer du sein dans cette région. Ces estimations pourraient être utilisées pour informer les autorités de santé publique et améliorer les modèles d'accès au traitement du cancer du sein en Afrique subsaharienne.

L'évaluation de la complétude des CRA et FDA de pièces opératoires de cancer du sein, au cours de la troisième étude, a été pour nous une occasion d'évaluer la coordination des différents acteurs de la prise en charge du cancer du sein au Bénin. Cette étude nous a permis de mettre en évidence, indirectement, les problèmes de coordination au sein des équipes de soins. Une des limites de cette étude est de n'avoir exploré que la communication entre les pathologistes et les médecins traitants ; et un seul aspect de cette communication (la rédaction des documents et compte rendus). Elle devra donc être complétée par des études évaluant plus complètement les interactions entre les différents praticiens intervenant dans les RCP de prise en charge du cancer du sein.

Malgré ces limites, l'étude revêt un intérêt significatif. À notre connaissance, notre étude est la première au Bénin à évaluer les FDA et les CRA. Les résultats pourraient servir de référence pour la réalisation d'études plus approfondies ; et contribuer à l'amélioration des pratiques et de la survie des patientes.

IV.3. Discussion des résultats

IV.3.1. Survie des femmes atteintes d'un cancer du sein au Bénin et en ASS

Dans cette thèse, la survie à 5 ans des patientes atteintes d'un cancer du sein à Cotonou était de 48,5 % dans les hôpitaux de niveau tertiaire et de 37 % selon les données du Registre des Cancers de Cotonou (registre populationnel). Nous avons estimé cette survie à 44 % pour l'Afrique au Sud du Sahara (revue systématique et méta-analyse). Cette survie relativement faible a été confirmée dans plusieurs études réalisées en d'ASS.

Ainsi Joko-Fru et al. dans une étude regroupant 2558 patientes de 12 pays d'ASS (Bénin, Côte d'Ivoire, Ethiopie, Kenya, Mali, Ile Maurice, Mozambique, Namibie, Seychelles, Afrique du Sud, Uganda et Zimbabwe) a obtenu une survie à 5 ans de 52,3% (Joko-Fru et al., 2020).

Dans une autre étude réalisée par Steady Chasimpha et al. dans 5 pays anglophones d'ASS (Nigéria, Afrique du Sud, l'Uganda et la Zambie), la survie était encore plus faible. Dans cette étude, la survie à 3 ans était de 55 % chez les femmes séronégatives (Chasimpha et al., 2022). La survie à 3 ans des femmes séropositives au VIH /SIDA était encore plus faible et estimée à 46% (Chasimpha et al., 2022). L'impact de l'infection par le VIH SIDA sur la survie des patientes atteintes de cancer du sein n'a pas été exploré dans cette thèse, mais il existe des signes d'alerte lorsqu'on sait que l'ASS est l'une des régions du monde les plus concernées par l'infection au VIH-SIDA. Ainsi l'ONUSIDA estime que l'Afrique abrite près de 70% des adultes et 80% des enfants vivant avec le VIH, et supporte les trois quarts du fardeau des plus de 20 millions et plus de personnes décédées dans le monde depuis le début de l'épidémie (Nations Unies, 2001). L'ASS continue de subir la double charge des MNT comme le cancer du sein, et des maladies infectieuses comme le VIH SIDA. Cette situation a été aggravée par la pandémie liée au COVID 19. En Afrique du sud par exemple, l'impact de COVID-19 sur les services de traitement du cancer du sein s'est fait sentir à la fois au niveau du diagnostic et des délais d'intervention chirurgicale ; avec notamment une chute du nombre de cas diagnostiqués et une diminution globale des chirurgies mammaires pratiquées (Van Wyngaard et al., 2022).

La survie des femmes atteintes d'un cancer du sein est nettement plus élevée en Europe et en Amérique du nord. Dans une étude ayant inclus 18 962 femmes atteintes d'un cancer du sein dans 7 états américains et 12 pays européens, la survie à 5 ans était de 81 % en Europe et de 84 % aux États-Unis. La survie en Europe du Nord, de l'Ouest et du Sud (81 à 84 %) était similaire à celle des États-Unis (84 %), mais elle était plus faible en Europe de l'Est (69 %) (Allemani et al., 2013).

La survie semble corrélée au niveau d'index de développement, les patientes vivant dans les pays ayant un index de développement élevé ayant une meilleure survie. En fait, les taux de mortalité par cancer dans les pays africains ne sont pas comparables à ceux des pays à revenu élevé et atteignent des proportions inacceptables (Vanderpuye et al., 2017). De fait, les taux de survie actuellement observés dans les pays d'ASS comme le Bénin, sont équivalents à ceux observés aux USA dans les années 1940 (Birnbaum et al., 2018).

IV.3.2. Age au diagnostic

Dans une étude hospitalière, réalisée chez 262 femmes ougandaises, Galukande et al. avaient trouvé une moyenne d'âge de 45 ans (Galukande et al., 2015), similaire à celle de notre étude. Joko-Fru et

al, dans une étude incluant 809 femmes provenant de 11 registres du cancer basés sur la population (Abidjan, Bamako, Brazzaville, Bulawayo, Cotonou, Eldoret, Kampala, Maputo, Namibie et Nairobi, Addis-Abeba) en ASS, avait retrouvé pour âge médian 48 ans (Joko-Fru et al., 2021). Bane avait retrouvé 46,9 ans, dans son étude portant sur 42 patientes au Centre Hospitalier Mère- Enfant le Luxembourg de Bamako, Mali (Bane, 2011). Au Soudan, dans l'étude de Muddather et al, pour les 225 cas, l'âge médian était de 45 ans (Muddather et al., 2021). Dans l'étude de Ly et al. faisant l'état des connaissances sur le cancer du sein chez la femme de l'Afrique sub-saharienne, l'âge moyen au diagnostic variait de 42 à 53 ans selon les régions (Ly et al., 2011).

Ainsi, les études réalisées en ASS insistent sur le jeune âge des patientes. Cette relative jeunesse contraste avec les données de la littérature occidentale dont sont issues la plupart des recommandations pour le dépistage du cancer du sein en population générale. Pourtant, les recommandations occidentales préconisant la mammographie de dépistage chez les femmes entre 50 et 74 ans sont encore largement utilisées sur le continent. La détermination de l'âge du diagnostic des cancers du sein en ASS aidera à l'adaptation de ces recommandations.

Dans l'étude de Dos Santos et al, réalisée en Pologne, sur 315278 patientes, l'âge médian était de 60 ans (Dos Santos et al., 2023). Dans les études réalisées en Europe occidentale, l'âge moyen du diagnostic du cancer du sein est largement plus élevé. Ilic et al., sur 163694 cas de cancer de sein lors d'une étude en Autriche, avait trouvé pour âge médian 64 ans (Ilic et al., 2022).

Selon Hemminki et al, l'âge bas au diagnostic des cancers du sein dans les pays en voie de développement peut s'expliquer par trois théories :

- la première ligne se réfère principalement à des différences biologiques,
- la seconde fait référence à un effet de cohorte en rapport à la forte proportion de sujets jeunes dans les populations de ces pays,
- la troisième à l'enregistrement incomplet du cancer chez les personnes âgées (les particularités épidémiologiques du cancer du sein chez la personne âgée dans les pays à index de développement moyens et faible, et du cancer en général dans cette population, sont détaillées dans un article auquel nous avons contribué (**annexe 2**)).

IV.3.3. Stade au diagnostic

La majorité des patientes de cette étude étaient diagnostiquées au stade tardif (III et IV). Cette tendance à un stade tardif au moment du diagnostic a été confirmée dans plusieurs séries subsahariennes. Ainsi, dans une étude hospitalière réalisée par Kantelhardt et al, en éthiopie sur 1070 femmes, les stades III représentent 71 % (Kantelhardt et al., 2014). Kakudji et al, dans leur étude portant sur 138 patientes en Afrique du Sud, avait trouvé un nombre significativement élevé de patientes se présentant à un stade III (33,3%) (Kakudji et al., 2020). En Côte d'Ivoire, Toure et al,

avaient retrouvé sur 350 patientes, 78 % de stade tardif au diagnostic, répartis en cancer localement avancé (63,7 %) et métastatique d'emblée (14,3 %) (Toure et al., 2013).

Le diagnostic semble plus précoce en Afrique du Nord où Benbakhta et al, dans une étude au Maroc, sur 200 patientes avaient estimé que le diagnostic a été fait dans 13,5 % des cas au stade I, 40,5 % au stade II, 43 % au stade III et 3 % au stade IV (Benbakhta et al., 2015).

Seneviratne et al, dans une étude en Nouvelle-Zélande, sur 12390 femmes, ont mis en évidence que plus d'un tiers (33,7 %) des cancers chez les femmes du Pacifique et un quart des cancers chez les Maoris (26,1 %) étaient avancés (stade III ou IV) au moment du diagnostic, contre moins d'un cinquième en Nouvelle-Zélande, en Europe (18,3 %) et en Asie (17,7 %) (Seneviratne et al., 2016).

IV.3.4. Retard diagnostique

Dans notre étude, le délai médian de consultation était de 60 jours avec IIQ = [14 jours ; 180 jours]. La majorité des patientes avaient consulté avant 06 mois (76,4%). D'autres études menées en Afrique de l'Ouest retrouvent des délais relativement allongés. Ainsi, Touré et al. en Côte d'Ivoire, Benbakhta et al. au Maroc et Sano et al. au Burkina-Faso rapportaient respectivement 10 mois, 65 jours et 4 mois pour le délai de consultation (Benbakhta et al., 2015; Sano et al., 1997; Toure et al., 2013).

Les délais de consultation sont nettement plus faibles dans les pays à index de développement élevé. Revaux et al. à Paris en 2014 avaient retrouvé un délai de 9 jours (Revaux et al., 2014).

Les facteurs associés au diagnostic tardif du cancer du sein varient d'un pays à l'autre. En Ethiopie, les facteurs associés au diagnostic tardif étaient la consultation tardive, les retards liés au système de santé, le sexe féminin, la résidence en zone rurale ; l'existence d'une masse mammaire comme principal symptôme, l'existence de comorbidités, le recours à la médecine alternative, la faible connaissance du cancer du sein, le manque de confiance aux soins hospitaliers (Agodirin et al., 2021; Tesfaw et al., 2021).

La crise sanitaire liée au COVID 19 a aggravé le problème du diagnostic tardif des cancers du sein en ASS.

Au Nigéria par exemple, le nombre de patients nécessitant une chimiothérapie néoadjuvante systémique a augmenté de façon spectaculaire après la pandémie avec des stades avancés du cancer du sein au moment de la présentation (Joseph et al., 2022).

IV.3.5. Facteurs pronostiques

L'avènement de nouveaux moyens diagnostiques et la définition de nouveaux facteurs pronostiques et prédictifs a révolutionné les référentiels de prise en charge des cancers du sein, entraînant un bénéfice significatif en termes de survie, tant en survie globale qu'en survie sans maladie ou sans

récidive. Ces avancées vont de la détection précoce et la mise en évidence des lésions infracliniques à l'immunothérapie des cancers du sein triple-négatifs localement avancés ou métastatiques, ce qui a nettement amélioré le pronostic notamment dans les pays développés (Toure et al., 2013).

Dans cette étude, notre modèle était basé sur la mortalité / survie globale. Il existe d'autres modèles notamment ceux basés sur la survie sans récidive. En effet certaines formes de cancer du sein (notamment les cancers du sein hormono-dépendants et ceux surexprimant HER2) peuvent autoriser une survie de plusieurs années même après l'apparition de métastases. Dans de telles situations les modèles basés sur la survie sans récidive pourraient être un meilleur reflet du contrôle de la maladie. Ces modèles basés sur la survie sans récidive sont toutefois plus difficiles à étudier dans les pays à ressources limitées comme le Bénin ; la mise en évidence de la récidive nécessitant des moyens diagnostiques peu accessibles en ASS (Tomodensitométrie, Tomographie par émission de positron, Imagerie par Résonance Magnétique, Scintigraphie, biopsies guidées par l'imagerie, etc).

Toutefois, les modèles basés sur la mortalité demeurent les plus utilisés. Ainsi dans une revue systématique publiée en 2019, sur les 96 modèles inclus, 58 prédisaient la mortalité, 23 le récidive et 7 étaient mixtes. La méthode la plus couramment utilisée pour l'élaboration du modèle est la régression des risques proportionnels de Cox ($n = 32$) (Phung et al., 2019). Nous avons utilisé la même méthode dans cette étude.

Par ailleurs aucun de ces modèles n'avait été développé en Afrique ; ces modèles ont été développés en Europe ($n = 25$), en Asie ($n = 13$), en Amérique du Nord ($n = 12$) et en Australie ($n = 1$) (Phung et al., 2019). Ce constat rappelle la nécessité de mener des études sur le continent Africain afin d'identifier d'éventuels facteurs prédictifs spécifiques.

Les principaux facteurs pronostiques identifiés par les différents modèles étaient : l'invasion lymphatique, ($n = 49$), la taille de la tumeur ($n = 42$), le grade de la tumeur ($n = 29$), l'âge au moment du diagnostic ($n = 24$), et le statut des récepteurs d'œstrogènes ($n = 21$). Ces facteurs ont également été identifiés dans nos études.

La taille de la tumeur et l'invasion lymphatique associé à la présence ou non de métastase contribuent à définir le stade (AJCC). Le stade est donc le principal facteur pronostic : de plus à l'inverse de l'âge au diagnostic et du statut des récepteurs à l'œstrogène est modifiable notamment par la mise en place de programmes de dépistages adaptés.

D'autres biomarqueurs pronostiques et prédictifs dans le cancer du sein ont été étudiés: les mutations du gène ESR1, la surexpression du HER2, l'expression des récepteurs à la progestérone, les marqueurs tumoraux (ACE, CA-15-3, et CA125), la recherche de cellules tumorales circulantes (CTC) et l'ADN tumoral circulant (ADNtc), l'index de prolifération Ki67, la Cycline D1, le Micro

ARN (miRNA), le « Programmed death ligand-1 » (PD-L1), les lymphocytes infiltrant la tumeur (TILs) (Tarighati et al., 2023).

IV.3.6. Profil moléculaire du cancer du sein au Bénin et en ASS

Le CSTN est un type moléculaire de cancer du sein réputé agressif car ayant une plus grande tendance à métastaser dans les organes vitaux tels que le cerveau ; et est généralement moins accessible au traitement en raison de l'absence d'efficacité des thérapies ciblées et de l'hormonothérapie (Jin et al., 2018). Même si le développement récent de molécules d'immunothérapie telle que le Pembrolizumab ouvre des lueurs d'espoir pour les patientes ayant des formes métastatiques et localement avancées, le CSTN demeure le type moléculaire de cancer du sein ayant le pire pronostic.

La forte proportion de CSTN retrouvée dans l'étude hospitalière a été relevée dans plusieurs études en ASS. Au Cameroun, selon Atangana et al, les CSTN avec une proportion de 37,9 %, étaient le sous type moléculaire majoritaire des cancers du sein (Atangana et al., 2017). Ly et al. en 2012 au Mali ont retrouvé une proportion de 46,5% de CSTN (Ly et al., 2012). Les CSTN représentaient en outre 55% des cancers du sein de l'étude de Huo et al. menée au Sénégal et au Nigéria (Huo et al., 2009). Cette proportion culminait à 58,5% au Ghana (Der et al., 2015).

La prévalence du CSTN semble nettement plus basse dans les autres régions du monde. En Afrique du nord par exemple, la prévalence des CSTN était estimée entre 16,5 et 17,5 % au Maroc (Akasbi et al., 2011; Rais et al., 2012) ; et entre 19,9 et 21,6 % en Algérie (Gaceb et al., 2018; Souad et al., 2018).

En Chine, Zhang et al. ont obtenu une proportion de 20%. En Californie (USA), selon les données du registre des cancers, la prévalence du CSTN est de 12,5% selon Bauer et al. (Bauer et al., 2007). Cette forte prévalence du CSTN dans notre étude et dans les séries d'Afrique de l'Ouest est cohérente avec la prévalence élevée du cancer du sein triple négatif observée dans les populations ayant une forte ascendance ouest-africaine (Moreno-Estrada et al., 2013; Scott et al., 2019; Zakharia et al., 2009) dans les Caraïbes (Hercules et al., 2022; Ragin et al., 2018) et en Amérique du Nord (DeSantis et al., 2017).

Les études américaines basées sur les origines ethniques permettent d'établir la relation entre origine ethnique et fréquence du CSTN. Ainsi, la prévalence du cancer du sein triple négatif chez les femmes blanches non hispaniques a été estimée à 8%, alors qu'elle était de 15% chez les femmes noires non hispaniques (Hercules et al., 2022). Des disparités plus frappantes ont été mises en évidence : la prévalence du cancer du sein triple négatif a été estimée à 8% et 25%, respectivement

chez les femmes blanches et noires, dans une population londonienne en se basant sur les données d'un registre du cancer au Royaume-Uni (Jack et al., 2013).

Ces fréquences élevées de cancer du sein triple négatif en Afrique, dans la diaspora africaine, et chez les afrodescendantes sont préoccupantes et font du cancer du sein la plus remarquable des inégalités en oncologie basées sur l'ethnicité (Newman & Kaljee, 2017).

Schématiquement, à notre avis, trois hypothèses pourraient expliquer la fréquence du CSTN dans les populations noire d'ASS :

- d'abord des susceptibilités génétiques : Une étude réalisée sur une cohorte montre un sous-ensemble de gènes associés à l'Afrique et des différences dans le tissu mammaire normal ; mais également que les profils immunologiques associés aux tumeurs sont spécifiques chez les patientes d'origine africaine (Martini et al., 2022),

- la structure de la population Africaine, qui est particulièrement jeune ; étant donné que le jeune âge au moment du diagnostic (moins de 40 ans) a déjà été associé à des cancers du sein triple négatifs et HER2+ ainsi qu'à une évolution clinique plus agressive (Gómez-Flores-Ramos et al., 2017),

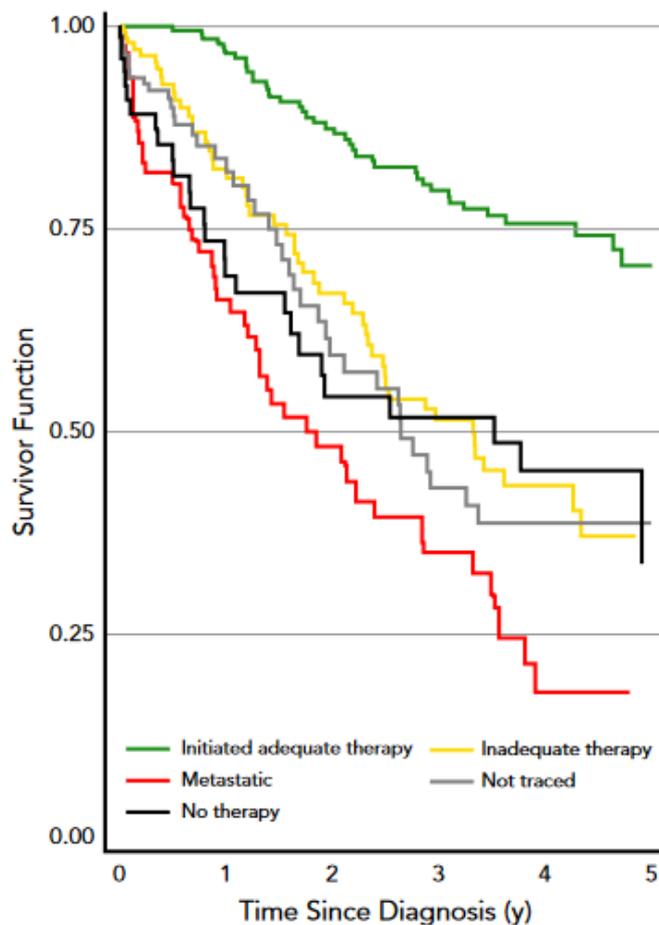
- Les faux négatifs à l'immunohistochimie (IHC), le prélèvement et le traitement des échantillons ne sont pas accessibles de la même manière et ne sont pas non plus réalisés de manière uniforme sur le continent africain. La fixation des échantillons, la durée de conservation des échantillons et d'autres variables préanalytiques de l'IHC ont un impact sur la précision des résultats (Gown, 2016). Ainsi, il a été estimé que jusqu'à 20 % des résultats de l'IHC dans le monde sont inexacts en raison de ces variables pré-analytiques (Agrawal et al., 2018).

Toutefois, dans une autre étude, Phipps et al. montrent une association positive entre l'IMC et le cancer du sein triple négatif post-ménopausique (Phipps et al., 2011). De plus dans les études nord-américaines, le cancer du sein triple négatif est principalement associé non seulement à l'origine ethnique afro-américaine, mais également au statut de pauvreté et à un âge plus jeune au moment du diagnostic, un grade plus élevé, un stade plus avancé de la maladie, des antécédents familiaux de cancer du sein, des indices mitotiques élevés et aux mutations BRCA1 (Bethea et al., 2016; Boyle, 2012; Williams et al., 2016). Tous ces facteurs pourraient également contribuer à la fréquence plus élevée du cancer du sein triple négatif en ASS.

IV.3.7. Capacité du système de santé

La capacité du système de santé et notamment, la disponibilité des thérapies adjuvantes est critique pour réduire la mortalité liée au cancer du sein. Par exemple, aux États-Unis, les taux de mortalité par cancer du sein ont diminué de 36 % entre 1989 et 2012 essentiellement en raison de l'amélioration combinée du dépistage précoce et du traitement systémique adjuvant (Birnbaum et al., 2018).

A titre d'illustration de ce paragraphe, nous avons contribué à une publication qui avait pour but de décrire le diagnostic, le traitement et le pronostic du cancer du sein en Afrique subsaharienne. 809 patientes ont été aléatoirement tirées des bases de données de 11 registres du cancer basés sur la population urbaine de 10 pays (Bénin, Congo, Côte d'Ivoire, Éthiopie, Kenya, Mali, Mozambique, Namibie, Namibie, Ouganda et Zimbabwe). Cette étude a permis de montrer que lorsque le traitement du cancer du sein ne respectait pas les recommandations, la survie des patientes était comparable à celles n'ayant reçu aucun traitement (**Figure 8**).



	Number at risk					
	0	1	2	3	4	5
Initiated adequate therapy	198	170	132	107	61	28
Inadequate therapy	150	73	53	39	17	5
Metastatic	85	45	25	16	5	0
Not traced	175	51	29	21	5	2
No therapy	76	32	21	19	11	3

Figure 8: Survie globale des patientes atteintes d'un cancer du sein dans 10 pays d'ASS en fonction du traitement reçu (Joko-Fru et al., 2020)

Brandão et al. (Brandão et al., 2021) ont montré que rien que l'introduction des RCP à l'hôpital central de Maputo (un centre hospitalier universitaire) en mars 2016 a contribué à une réduction de 53 % de la mortalité due au cancer du sein.

Notre étude a mis en évidence le manque de ressources en matière de diagnostic et de traitement du cancer comme l'un des principaux obstacles rencontrés dans les hôpitaux des pays d'ASS. Ces résultats corroborent ceux obtenus par Yekpè et al. (Yekpe Ahouansou et al., 2022) dans leur enquête menée sur l'accessibilité à l'imagerie dans la prise en charge des cancers du sein dans huit (08) hôpitaux du niveau central et intermédiaire du système sanitaire béninois. Les auteurs n'avaient retrouvé que deux formations sanitaires disposant d'un tomodensitomètre fonctionnel.

En outre, dans leur enquête menée en 2016 sur la disponibilité des services de pathologie dans 17 pays d'Afrique au Sud du Sahara (y compris le Bénin), Ziegenhorn et al. (Ziegenhorn et al., 2020) avaient révélé d'importantes disparités dans la disponibilité des ressources pour le diagnostic du cancer. Une autre enquête menée par l'AIEA en 2020 avait montré que près de la moitié des pays africains (26/54), dont le Bénin, ne disposaient pas d'une unité de radiothérapie (Elmore et al., 2021). Il urge donc de renforcer la capacité des hôpitaux publics du Bénin à diagnostiquer et à traiter le cancer en investissant dans l'acquisition d'équipements médicaux.

L'équipement et les infrastructures ne sont pas les seuls défis du système de santé des pays d'ASS pour la prise en charge du cancer du sein. Il est important de noter que le Bénin, comme de nombreux autres pays d'Afrique, souffre d'un manque criard en ressources humaines spécialisées en oncologie. Plusieurs études ont même révélé des disparités significatives en termes de disponibilité d'oncologues médicaux entre les pays d'Afrique du Nord et du Sud, et les pays d'Afrique de l'ouest et du centre (Brahmi et al., 2017).

IV.3.8. Mortalité liée au Cancer du sein en ASS : la plus remarquable des disparités en oncologie basée sur l'ethnicité

Le cancer du sein en ASS pose un problème d'équité car bien que l'incidence y soit la plus faible au monde, la mortalité y est la plus élevée, témoignant d'une survie particulièrement faible (Joko-Fru et al., 2021). Plusieurs particularités expliquent la surmortalité par cancer du sein des femmes d'ASS.

La première particularité serait spécifique aux femmes noires : une étude menée aux États-Unis, en 2012, a montré que la mortalité par cancer du sein est 42 % plus élevée chez les Afro-Américaines que chez les Américaines blanches (DeSantis et al., 2016)

Cette particularité est retrouvée chez les femmes noires et afrodescendantes vivant dans les pays occidentaux : elles sont réputées développer des cancers du sein plus agressifs, plus létaux et à un âge plus jeune que ceux des femmes issues d'autres origines ethniques vivant dans ces mêmes régions. Pour Newman et Kaljee, « le cancer du sein est la plus remarquable des disparités en oncologie basées sur la race » (Newman & Kaljee, 2017).

Les femmes noires vivant en ASS devront faire face à des facteurs délétères supplémentaires (Gnangnon, 2023):

- (i) des considérations socioculturelles spécifiques et péjoratives (le cancer du sein et son traitement sont encore tabou ou stigmatisant dans certaines communautés) ;
- (ii) l'absence de programmes de dépistage organisés dans de nombreux pays d'ASS ;

(iii) la faible accessibilité économique et géographique aux moyens de diagnostic et de traitement, qui a été aggravée par la pandémie liée au covid 19 et plus récemment les différentes crises à l'échelle globale ;

(iv) les crises et l'instabilité militaro-politiques chroniques dans certains pays.

Ces facteurs constituent des obstacles insurmontables pour les femmes rurales, le plus souvent très pauvres et habitant dans les déserts médicaux du continent africain.

IV.3.9. De l'urgence de réduire la mortalité liée au cancer du sein en ASS

Selon la commission du *Lancet Oncology*, sans interventions rapides, la mortalité par cancer en ASS pourrait doubler d'ici 2030 (Ngwa et al., 2022). Il est de fait urgent d'agir pour enrayer cette crise croissante de la mortalité par cancer, notamment le cancer du sein.

Bien que l'incidence du cancer du sein en ASS soit parmi les plus faibles au monde, le fardeau du cancer dans la région devrait significativement augmenter dans les prochaines années pour plusieurs raisons (Pace & Shulman, 2016).

- la croissance démographique particulièrement rapide en ASS

-une diminution du fardeau des maladies infectieuses qui va de pair avec l'allongement de l'espérance de vie

-des changements dans les habitudes des populations les exposant de plus en plus aux facteurs de risque du cancer.

Cette augmentation de l'incidence des cancers du sein alors que le système de santé des pays d'ASS est caractérisé par (i) un accès limité aux soins infirmiers et à la chirurgie, (ii) un accès insuffisant à la radiothérapie, (iii) la faible disponibilité des thérapies systémiques classiques et modernes (Vanderpuye et al., 2017), pourrait se traduire, si rien n'est fait, par une hécatombe.

Il s'agira d'abord de développer ou de mettre à jour les plans nationaux de lutte contre le cancer dans chaque pays tout en définissant des itinéraires permettant de réduire les diagnostics manqués et les références tardives, notamment dans les zones rurales et défavorisées (Gourd & Collingridge, 2022). Une approche synergique consisterait à étendre la couverture sanitaire universelle afin d'intégrer les cancers, tout au moins ceux spécifiques aux couches sociales vulnérables (femmes, enfants), dans les prestations essentielles.

Parallèlement, l'amélioration de l'accès aux soins oncologiques pourrait prendre en compte une subvention de la radiothérapie et des thérapies systémiques telles que la chimiothérapie, l'hormonothérapie, les thérapies ciblées et l'immunothérapie (indisponible dans de nombreux pays d'ASS).

IV.3.10. Politiques pour la réduction de la mortalité du cancer du sein en Afrique Subsaharienne

La lutte mondiale contre le cancer du sein est une question d'équité entre les sexes et les droits de l'homme (World Health Organization, 2023). Les femmes jouent un rôle central dans la société ; protéger les femmes contre le cancer du sein, c'est aussi protéger leurs familles, leurs communautés et l'économie dans son ensemble (World Health Organization, 2023). De plus, l'incapacité des pays d'ASS à réduire la mortalité liée au cancer du sein constitue un frein à l'atteinte de l'ODD 3 (*Objectif de Développement Durable - Santé et Bien-Être pour tous*, 2023)

En effet, la mortalité liée au cancer du sein affecte disproportionnellement les patients dans les pays en voie de développement. Ainsi, selon l'Initiative Mondiale sur le Cancer du Sein (Global Breast Cancer Initiative - GBCI) de l'OMS, sur 10 patients atteints de cancer, 5 ans après le diagnostic, 9 seront encore vivant s'ils sont diagnostiqués dans un pays à index de développement élevé; 6 s'ils sont diagnostiqués en Inde ; et seulement 4 en Afrique du Sud (World Health Organization, 2023). De plus, si les tendances actuelles restent inchangées, le fardeau du cancer du sein devrait passer à 2,74 millions de nouveaux cas et 857 000 décès par an d'ici à 2030, et à 3,19 millions de cas et 1,04 million de décès d'ici à 2040 ; les impacts les plus dévastateurs étant attendus dans les pays à index de développement les moins élevés comme ceux d'ASS (International Agency for Research on Cancer, 2024)

Ces inégalités à l'échelle mondiale peuvent-être expliquées par 3 facteurs principaux inhérents au pays d'ASS :

- le diagnostic tardif
- les défaillances du système de santé marqué par une insuffisance des moyens de diagnostic et de traitement
- l'incapacité à inclure le cancer du sein dans la couverture santé universelle (World Health Organization, 2023).

Il est donc urgent de réduire la mortalité liée au cancer du sein en ASS. Cette réduction ne peut se concevoir sans la mise en place de politiques ciblant d'une part une réduction de l'incidence du cancer du sein en ASS et d'autre part, ses facteurs pronostiques.

Bien que l'incidence du cancer du sein en ASS soit actuellement parmi les plus faibles au monde, les projections prévoient une augmentation rapide de cette incidence. L'un des facteurs clés de l'augmentation de l'incidence du cancer du sein en Afrique au Sud du Sahara est l'adoption croissante d'un mode de vie et de comportements occidentaux entraînant des modifications du régime alimentaire, un âge de procréation plus tardif et une réduction de l'activité physique. Cette tendance à l'occidentalisation des modes de vie sera probablement accélérée par l'exode rural, l'urbanisation

des zones rurales et l'amélioration plus générale des conditions socio-économiques des populations (Azubuiké et al., 2018).

De plus, l'ASS est l'une des régions du monde avec les plus fortes projections de croissance démographique (The World Bank Group, 2024).

Il importe de renforcer les politiques de prévention primaire des maladies non transmissibles sur le continent. Pour résoudre les problèmes de mise en œuvre, les Ministères en charge de la santé, l'OMS et d'autres partenaires techniques et financiers doivent mettre en place des stratégies de suivi fiables concernant la consommation nocive d'alcool, les mauvaises habitudes alimentaires, l'inactivité physique et le tabagisme et ; créer un système de santé capable de garantir que ces politiques sont mises en œuvre et suivies d'effets (Kassa & Grace, 2022).

D'autres actions et politiques de santé publique doivent être entreprises pour cibler les facteurs pronostiques. Les plus importants mis en évidence dans cette thèse sont le stade tardif au diagnostic et le manque de capacité des systèmes de santé. Des stratégies, éprouvées dans les pays à index de développement élevé ont permis au cours des dernières décennies, de réduire de 40 %, la mortalité liée au cancer du sein et peuvent servir de modèle aux pays d'ASS.

L'Initiative Mondiale contre le Cancer du Sein (Global Breast Cancer Initiative - GBCI), lancée par l'OMS en 2021, et à laquelle nous avons contribué au cours de cette thèse, a pour objectif de fournir aux gouvernements, des orientations sur le renforcement des systèmes de santé pour le cancer du sein (World Health Organization, 2022).

La GBCI prône une politique basée sur 3 piliers :

-Pilier 1 : promotion de la santé pour une détection précoce

Par l'éducation à la santé publique afin d'améliorer la sensibilisation aux signes et aux symptômes, ainsi qu'à l'importance de la détection et du traitement précoces

-Pilier 2 : diagnostic rapide

L'éducation du public et des professionnels de la santé sur les signes et les symptômes du cancer du sein au stade précoce, afin que les femmes soient orientées vers des services de diagnostic le cas échéant

-pilier 3 : prise en charge intégrée

Des services centralisés ; étant donné que la prise en charge du cancer nécessite un certain niveau de soins spécialisés (World Health Organization, 2023).

Il est important de retenir, que, au-delà de ces grands axes prônés par la GBCI, des actions simples au quotidien peuvent nettement améliorer la survie des patientes à l'échelle d'un hôpital, d'une ville ou d'un pays. Par exemple, l'implémentation de RCP au Mozambique a induit une baisse de 53 %

de la mortalité chez les patientes atteintes d'un cancer du sein au stade précoce et s'est avérée rentable (Brandão et al., 2021). Ces résultats confirment que des politiques simples et peu coûteuses peuvent avoir un impact substantiel sur la survie des patientes atteintes d'un cancer du sein en ASS.

En outre, un investissement massif dans la formation des ressources humaines spécialisée en oncologie, en utilisant au besoin des technologies innovantes (e-learning) pour pallier la rareté des enseignants sur le continent (Domgue et al., 2023) s'avère nécessaire pour prévenir des millions de décès évitables à l'horizon 2030 (Ngwa et al., 2022).

Chapitre V. PERSPECTIVES

Au cœur de cette recherche résident des interrogations cruciales qui éclairent les multiples facettes du fardeau du cancer du sein au Bénin et en Afrique au Sud du Sahara (ASS). Ces questions sont d'une importance capitale pour l'amélioration des politiques de santé et des pratiques cliniques.

Dans ce chapitre, nous nous attelons à explorer trois axes :

- Tout d'abord, nous nous pencherons sur les facteurs qui sous-tendent le diagnostic tardif et l'accès au traitement des cancers du sein au Bénin et dans la région Afrique de l'OMS, éclairant ainsi les obstacles et défis systémiques, socio-culturels, financiers et logistiques qui entravent une détection précoce et efficace de la maladie et influencent les comportements de dépistage et l'accès aux soins de santé.
- Ensuite, nous examinerons le rôle potentiel des susceptibilités génétiques dans le pronostic des cancers du sein au Bénin. Nous nous intéresserons notamment à l'identification des variants génétiques spécifiques qui pourraient être associés à un pronostic péjoratif.
- Enfin, nous aborderons la question cruciale de la coordination des soins, en explorant les stratégies innovantes et les solutions technologiques pour renforcer les capacités de prise en charge, et la formation des professionnels de la santé en particulier dans les régions rurales défavorisées où les ressources humaines sont souvent limitées.

Nous nous poserons plus spécifiquement les questions suivantes :

1-Comment améliorer l'accès aux traitements systémiques oncologiques pour les pays en voie de développement comme ceux d'Afrique au Sud du Sahara ?

2- Comment améliorer la formation des professionnels de santé impliqués dans la prise en charge du cancer du sein en Afrique au Sud du Sahara ?

3-Quels sont les facteurs qui expliquent le diagnostic tardif des cancers du sein au Bénin et en Afrique au Sud du Sahara ?

4-Des susceptibilités génétiques peuvent –elles expliquer le mauvais pronostic des cancers du sein au Bénin ?

5-Comment peut –on améliorer la coordination entre les médecins prenant en charge le cancer du sein et le cancer en général dans les pays d'ASS comme le Bénin qui manquent cruellement de ressources humaines qualifiées surtout dans les zones rurales défavorisées ?

Certaines de ces questions ont fait l'objet de publications auxquelles nous avons contribué ; les autres feront l'objets de protocoles d'études que nous exposons dans la suite de ce document.

V.I. Améliorer l'accès aux médicaments contre le cancer en général et le cancer du sein en particulier pour en réduire la mortalité

Dans de nombreuses régions du monde, comme en ASS, les traitements essentiels contre le cancer ne sont pas accessibles, abordables ou disponibles pour les patients qui en ont besoin.

Une nouvelle coalition pour l'accès aux médicaments oncologiques (ATOM), qui s'appuie sur des partenariats public-privé, vise à mettre des médicaments anticancéreux essentiels et des outils de diagnostic à la disposition des patients dans les pays à faible revenu et à revenu intermédiaire de la tranche inférieure.

Au sein du groupe de la « promotion 2021 des jeunes leaders » de l'Union Internationale Contre le Cancer (UICC), nous avons lancé sous la forme d'un éditorial, un appel générationnel à garantir un accès équitable aux traitements oncologiques.

Dans les pays, quel que soit le niveau de revenu, on observe souvent une inégalité face au cancer, où les autochtones, les minorités ethniques, les personnes âgées, les femmes, les personnes ayant un statut socio-économique faible, les personnes vivant en zone rurale et/ou qui n'ont pas d'éducation, ont souvent moins de chances de recevoir un traitement rapide et efficace et, par conséquent, sont plus susceptibles d'en mourir. L'accès limité aux ressources pour la prévention, le dépistage, la détection précoce, le diagnostic, le traitement et les soins palliatifs expliquent la plupart des variations mondiales, régionales et infranationales de la mortalité due au cancer et au cancer du sein en particulier.

SCIENCE IN SOCIETY

Ensuring Global Access to Cancer Medicines:
A Generational Call to Action

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Summary: Essential cancer treatments are not accessible, affordable, or available to patients who need them in many parts of the world. A new Access to Oncology Medicines (ATOM) Coalition, using public-private partnerships, aims to bring essential cancer medicines and diagnostics to patients in low- and lower middle-income countries.

We are a group of 10 individuals brought together by the Union for International Cancer Control's (UICC) Young Leaders Programme, with a shared goal of reducing the global burden of cancer. We live on six continents and work across the cancer control continuum—from public health, community outreach, clinical care, and survivorship to cancer research, advocacy, and health policy. Our experiences, and those of the cancer communities we serve, are remarkably diverse, and yet our concerns are collective. There have been staggering advances in cancer prevention, diagnosis, and treatment during our lifetime. Yet these remain out of reach for most of the world's population and for many of the communities where we live and work. This is unjust, and it cannot continue. Launched in 2022, the UICC-led Access to Oncology Medicines (ATOM) Coalition aims to bring essential cancer treatment to patients in low- and lower middle-income countries (LLMIC) and offers a chance for our generation to change course.

Cancer is a leading cause of premature death in every country in the world. Although cancer is often thought of as a disease predominantly afflicting people living in what the World Bank classifies as high-income countries (HIC), 70% of all cancer deaths this year will occur in low- and middle-income countries (LMIC; ref. 1). We know—and experience in our daily working lives—that where you live largely determines

whether you will develop a certain cancer, as well as have access to timely and quality diagnosis and treatment, and significantly affects your odds of survival (2, 3). Breast cancer, for example, is the most common cause of cancer death in women worldwide and responsible for the deaths of over half a million women living in LMICs each year. In the United States, Canada, and New Zealand, the 5-year overall survival rate after a breast cancer diagnosis is ~90% compared with only 66% in India and Malaysia, and less than 40% in Nigeria and Uganda (1). For children diagnosed with cancer, the differences are even more stark: 80% will survive a diagnosis of a childhood cancer in HICs compared with only 20% in LMICs (3). Within countries of all income levels, there is often another story of cancer inequity, whereby those who are Indigenous, a racial or ethnic minority, uninsured, older, female, of low socioeconomic status, or live in rural areas and/or are uneducated are often even less likely to receive timely, quality cancer treatment and, as a result, are more likely to die (4).

Two defining features of cancer in many LMICs are the advanced stage of cancer presentation and a higher stage-for-stage case fatality rate compared with wealthier countries (2). Limited access, affordability, and availability of resources for cancer prevention, screening, early detection, diagnosis, treatment, and palliation explain most of the global, regional, and subnational variation in cancer mortality (2). In many HICs, avoidable cancer deaths occur amidst a sea of plenty—in which there are high levels of availability and affordability of both essential and advanced cancer diagnostics and treatment, yet inequitable access and utilization persist (4). In contrast, in many LMICs, the availability and affordability of even basic cancer tests, such as biopsy for diagnosis and hormonal receptor testing in breast cancer, and treatments such as the hormonal therapy tamoxifen and the cytotoxic drug doxorubicin are major issues (2, 5). A recent survey of oncologists from 82 countries estimated that these two key breast cancer medicines were universally available in only 36% of LMICs (5). For the most part, cancer medicines remain prohibitively expensive, mired by patents, trade regulations, and pricing structures that do not account for a country's economic reality, closely resembling the production, procurement, supply chain, and delivery challenges that have shackled the ability of many LMICs to vaccinate their citizens during the COVID-19 pandemic.

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What constitutes an essential cancer treatment? For patients, any treatment that allows them to improve their odds of survival and quality of life after a cancer diagnosis might be considered essential. However, faced with limited resources, countries and health systems all over the world need to make difficult decisions about what treatments they do and don't cover, and what constitutes value (6, 7). In cancer care, the wide range of treatments, rapid pace of innovation, high prices, and variable clinical efficacy data, which may not be generalizable across contexts, systems, and populations (most cancer medicine trials are still conducted in HICs in predominantly European-ancestry patient populations) make the task of assigning value both philosophically and practically complex (8, 9). To help address this, the World Health Organization (WHO) publishes the WHO Model List of Essential Medicines (EML). Updated every 2 years, the EML currently includes 62 cancer medicines encompassing antineoplastic agents, hormonal treatments, immunomodulators, and targeted therapies (9, 10). The list is used by more than 150 countries to develop their own national essential medicines lists. Essential medicines are intended to be always available, of assured quality, and at prices individuals and/or the health system can afford. The EML considers disease burden, population health impact, efficacy, safety, and comparative cost-effectiveness in making its recommendations. A guiding principle of the list is that cost is not a reason to exclude a medicine if it will make a substantive improvement in population health or disease outcomes (10). The aspiration has long been that if a medicine is deemed essential by the WHO EML, prices should be reduced to improve access in markets where it is unaffordable (9). Despite this, it is estimated that over 50% of cancer medicines listed on the WHO EML in 2021 are unavailable in LMICs (5). Although many countries have made ambitious commitments to universal health coverage, cancer treatments (and diagnostics) are often too expensive to include, at least during initial expansion efforts. Many of those costs are then transferred onto patients and households who must pay for cancer care entirely out of pocket. This often leads to catastrophic expenditure (whereby the cost of the medication absorbs >40% of a household's expenses), impoverishment, and treatment abandonment (2, 11). For example, a study in eight Southeast Asian countries demonstrated that one in two patients diagnosed with cancer is pushed into economic hardship, and one in three households (33%) fell below the national poverty line within a year of a household member being diagnosed (11). A recent international survey of cancer treatments on the EML suggests household affordability is an even greater access barrier than availability in most LMICs (5).

Although the prices of other medicines on the WHO EML have fallen since its inception in 1977, cancer medicines have not followed suit. In 1987, around the same time many of us—the authors of this article—were born, the FDA approved the first antiretroviral therapy (ART) for the treatment of HIV/AIDS. Additional drugs and more effective three-drug combinations quickly followed. They were expensive and available in only a few HICs. As with many scientific breakthroughs for global health challenges, after ART came to market, a wide chasm grew between where the greatest burden of disease and death from HIV/AIDS were—on the African continent and in South and Southeast Asia—and where the treatment was—in

North America and Western Europe (12). In 2022, this is often what it feels like to work in global cancer control—to be starting at a gap that gets wider and wider with each new scientific discovery and with each diagnostic test or treatment brought to high-income markets. To see novel targeted and immunotherapies “melt away” advanced colorectal, lung, and skin cancers in Canada but to be faced with the task of treating women with breast cancer in Nigeria who lack access to breast imaging, biopsy, or hormone receptor testing, who cannot afford surgery and chemotherapy, and who live thousands of kilometers from the nearest radiation machine (2).

But we also know that this story can be different. Although we, as a group of UICC Young Leaders, were born in a time when a diagnosis of HIV/AIDS anywhere in the world was a swift and certain death sentence, we grew up in an age where HIV became a manageable chronic illness—if you had access to ART. The differential impact of this access in our communities and countries, and the sweeping social and economic impact of the HIV/AIDS epidemic, shaped many of our lives and our early interests in health care and health advocacy. In fact, it still shapes the health systems and the social and economic circumstances in several of the countries in which we work today. In our lifetime, and from our different vantage points, we have seen how HIV/AIDS activism, politics, and global partnership achieved what many believed to be socially, politically, and economically impossible only two decades ago (12). Antiretroviral medicines once deemed too expensive to purchase and too complex to deliver in low-resource settings are now taken by some 25 million people living with HIV in LMICs, 87% of all people who know their HIV status are on treatment, and 90% of them are completely virally suppressed (13). The cost of ART in LMICs dropped by as much as 99% in the decade between 1996 and 2006 through a combination of voluntary licensing agreements with pharmaceutical companies, generic competition due to the expiry of drug patents, the use of legal flexibilities in international trade rules, tiered pricing based on a country's gross national income, and other innovative financing mechanisms and partnerships (14). Recognizing that affordability is not the same as availability, precipitous falls in the cost of HIV treatment were coupled with the financing and implementation of effective “test and start” diagnostic and treatment delivery mechanisms—including those focusing on the type of “last mile” communities where many of us serve—alongside procurement, regulation, and monitoring processes (15). Similar stories are currently being written for human papillomavirus (HPV) vaccination (against HPV-associated cervical, oral, and anal cancers; ref. 16), hepatitis B virus vaccination (hepatitis B-associated liver cirrhosis and liver cancer; ref. 17), and direct-acting antivirals for hepatitis C (which have transformed treatment of the virus, and associated hepatocellular cancer and cirrhosis). We believe that it is possible to write this story for cancer too. In fact, we have never been closer.

This year, the UICC established a new and ambitious global partnership, the ATOM Coalition (18). The coalition's goal is to increase the availability and affordability of cancer medicines and diagnostics in LMICs and to increase country capacity and coordination to deliver these to patients who need them (Fig. 1). Although the ATOM Coalition is not the first initiative attempting to address access issues, it is the first to bring together many major stakeholders globally across the public



Figure 1. The Access to Oncology Medicines Coalition's three pillars of work. LLMICs, low- and lower middle-income countries.

and private sectors to act on both supply- and delivery-side challenges (Table 1). This includes the pharmaceutical, biotechnology, and diagnostic companies AstraZeneca, Becton Dickinson, BeiGene, Bristol Myers Squibb, Gilead, MSD, Novartis, Roche, Sanofi, and Thermo Fisher Scientific; the Medicines Patent Pool that negotiates with patent holders for voluntary licenses that permit lower cost manufacturers to distribute patented medicines in LLMICs and patent pooling; and organizations already working at the country level on access to medicines and cancer capacity building, such as The Max Foundation, Project ECHO, the American Society for Clinical Pathology, Direct Relief, the IDA Foundation, and others. As part of its work, the ATOM Coalition will support countries to systematically identify and address needs, gaps, and challenges at the systems level that limit availability and affordability, and aim to develop and implement sustainable, scalable access solutions. Many of the upstream barriers patients and health systems face accessing cancer medicines start beyond national borders and, as with ART, relate to international trade and intellectual property law, patents, licensing, regulation, manufacturing, and supply chains. At the country level, proper handling, supply monitoring, forecasting, and quality assurance are crucial, as is having the cancer and health system infrastructure in place to initiate, monitor, and complete a treatment course. The strength of the coalition includes the long-standing relationships, infrastructure, and track record that individual stakeholders already have both with countries and in many cases with each other, and its ability to act as a single negotiating mechanism rather than on

a country-by-country, organization-by-organization, or drug-by-drug basis. New financing and licensing mechanisms will be needed to lower the price of cancer medicines still on patent, as well as new medicines as they come to market including via voluntary licensing agreements with the Medicines Patent Pool (an official observer to the ATOM Coalition) that opened up access to HIV, hepatitis B, and tuberculosis medicines. However, some 70% of the cancer medications currently listed on the WHO EML are older off-patent therapies (9). Increasing local and regional production of cheaper generic and biosimilar medicines is one of the most pressing actions to address availability and affordability of those drugs already on the EML (9). Strengthening procurement, supply management, and quality assurance within a country's health system is then required to get medicines to patients.

Medicines are of course only one tool in the cancer control armamentarium and cannot close the cancer care gap on their own. Without affordable, available, and timely diagnostic tests—for example, those that stratify breast cancer by hormone sensitivity (e.g., estrogen receptor/progesterone receptor) and the targetable oncogene *HER2/neu* or identify targetable mutations in lung cancer [e.g., *EGFR* mutations for tyrosine kinase inhibitor (TKI) use] to ensure patients get the type of treatment they need—many of the medicines on the EML cannot be deployed safely or effectively (19). To address this, the coalition is also engaging a range of public and private stakeholders involved in the development and delivery of cancer diagnostics, biotechnology, and genomics. In addition, effective cancer treatment requires the coordinated

Table 1. Four areas in which action to improve access to cancer medicines is urgently needed and how the ATOM Coalition will address them

	Challenge	ATOM contributions
Production and supply of generics and biosimilars	The cost of brand-name cancer medicines is prohibitive, even when their patents have expired. Generics and biosimilars can substantially reduce costs but are underutilized in LMICs owing to limitations imposed by a lack of capacity in manufacturing, procurement, and regulation.	One of the three pillars of the Coalition includes making available more WHO EML generic and biosimilar cancer medicines over time by working with generic, biosimilar, and originator manufacturers to register and supply quality-assured essential cancer medicines at affordable prices in ATOM Coalition target countries.
Opening access to new and on-patent treatments	Newer and emerging cancer medicines are under patent and usually have a price set or informed by high-income markets, which relates to marketability rather than to the cost of innovation. This makes new and on-patent cancer medicines prohibitively expensive in LMICs, with little current mechanism or incentive for price adjustment or voluntary licensing.	The ATOM Coalition will focus part of its core work on securing an increasing number of patented medicines and new medicines in the pipeline from biopharma over time through a variety of channels, including donations, discounted pricing, and voluntary licensing.
Ensuring universal health coverage includes cancer care	Affordability at the individual patient and household level is a major barrier to accessing cancer care and initiating and completing treatment. Cancer care is often not included in publicly financed health benefit packages, resulting in catastrophic health expenditures and diminishing the impact of increased availability of medicines at the country level.	One of the areas that ATOM Coalition partners aim to deliver the greatest impact is by supporting governments in low- and lower middle-income countries to develop sustainable health financing, particularly to cover the investment in training the health workforce on the appropriate use of medicines, diagnostics capacity, and medicines for cancer treatment.
Embedding cancer within health system strengthening efforts	Cancer care is complex, multimodal, and delivered across a continuum. Multiple parts of the health system must function together to deliver timely, affordable, available, and quality care.	Under the second and third pillars, ATOM Coalition partners will further collaborate with local stakeholders and country governments to address the system-level barriers to access across the health system, including streamlining regulatory processes, forecasting, procurement, and funding; strengthening logistics and supply chain management; and implementing training and education programs for health care workers and supportive care staff.

delivery of multiple interventions within a population and health system, which go far beyond supplying medications. Although surgery is the mainstay of curative treatment for many solid malignancies, including breast, gastric, liver, and colorectal cancers, safe oncologic surgery is still not available in many parts of the world (20). Radiotherapy, which is unavailable or inaccessible in many LMICs, is critical for the treatment and locoregional control of many high-burden cancers and serves as an important means of palliating symptoms when curative treatment is not possible (21). Pathology and imaging are required for diagnosing and staging all cancers and for treatment planning but again, these critical services are often underdeveloped or out of reach for most patients (22). To realize the full potential of the ATOM Coalition, countries and the international community will need to address each of these pillars of cancer control at subnational, national, and international levels and along the cancer continuum. This includes prevention, screening, and early detection efforts; expansion of universal health coverage to ensure that the costs of cancer treatment are not borne by individual patients and their families; and investment in human resources, national and regional governance, and health systems leadership.

One clear lesson from HIV/AIDS is that investment in one part of the access equation can catalyze the growth of other components, and even entire health systems, when civil society demand, political will, financial and human resources, and underlying motivations align (12). One caution is that a singular focus on distributing medicines for a condition can distort health resource distribution and prioritization, especially when this occurs outside existing health systems. Because government prioritization and commensurate investment are key to ownership and sustainability, the ATOM Coalition will prioritize partnering with countries already committed to or engaged in improving cancer control.

Although the ATOM Coalition and the partnerships it has created represent an enormous stride forward in global cancer control, we are realistic about the challenges such initiatives face in increasingly complex national and global geopolitical and economic contexts. A recent example is the COVAX initiative, which aimed to accelerate the development and manufacture of COVID-19 vaccines and act as a global risk-sharing mechanism for pooled procurement and fair and equitable vaccine distribution for every country in the world (23). This included 92 LMICs that, through a Gavi (the Vaccine Alliance)-supported innovative financing mechanism, were to

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have access to donor-funded vaccines and country-delivery supports. Although COVAX successfully distributed over 1 billion vaccine doses, it fell significantly short of its target, and many of the LMICs it aimed to support had to find alternative ways to obtain vaccines. The enthusiasm for global solidarity that heralded the arrival of the COVAX initiative was tested during its subsequent implementation. Challenges faced included a lack of early financing for the initiative, hoarding of vaccines by HICs procured through direct bilateral agreements with pharmaceutical companies outside the COVAX mechanism, export restrictions on key vaccine components coupled with a lack of regional suppliers and manufacturers, and a reliance on an aid-financed mechanism for vaccine procurement in LMICs rather than intellectual property waivers and technology transfers to facilitate production outside of high-income regions (24). One of the main lessons of COVAX, which should be applied to all global initiatives, is that good intentions are not enough. Global solidarity must be hard-wired into the design, financing, and risk-pooling mechanism of coalitions such as the ATOM Coalition. Local ownership is key to implementation and sustainability. Success must be measured not in commitments but in actions. In fact, the ATOM Coalition is already translating its ambition into concrete outcomes. The announcement of the first-ever public health-oriented voluntary license of a cancer drug [the BCR/ABL TKI nilotinib for chronic myeloid leukemia (CML)] in October 2022 shows the promise and power of public and private sector collaboration (25). In HICs, patients with CML receiving TKI treatment achieve similar life expectancies to the age-matched general population (26). Despite being on the WHO EML, these treatments have been out of reach for most patients in LLMICs. Under the umbrella of the ATOM Coalition, the agreement between ATOM Coalition partners Novartis and the Medicines Patent Pool represents an exciting milestone for the cancer community and signals a real opportunity for more companies to consider engaging voluntary licenses to expand access to cancer medicines.

As the next generation of cancer advocates, professionals, and leaders, we stand committed to realizing a future for our patients and communities in which cancer diagnostics, medicines, and treatments are available, affordable, and accessible to all—a future where countries can develop, procure, produce, and deliver essential cancer medicines for their populations on an equitable footing, as partners in the global creation, dissemination, and delivery of cancer knowledge, resources, and care. We call upon patients, caregivers, civil society, political leaders, industry, private and public institutions, and the wider cancer and health community to commit to delivering on the goals of the ATOM Coalition. We are optimistic that within our lifetime we can end unjust and unnecessary differences in access to cancer care within and between our countries, leaving no one behind.

Authors' Disclosures

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V.2. L'utilisation de l'e-learning pour pallier le manque criard de ressources humaines spécialisées en oncologie mammaire en ASS

En plus de la disponibilité limitée du dépistage, du diagnostic et du traitement, la rareté d'une main-d'œuvre qualifiée est un obstacle majeur à la lutte contre les cancers en Afrique, et plus particulièrement le cancer du sein. Certains pays d'Afrique étant confrontés à une pénurie criarde de mentors et d'enseignants en oncologie, il s'avère indispensables de mutualiser et d'optimiser les ressources humaines disponibles. Les programmes d'apprentissage en ligne existants ayant été principalement réalisés en anglais, la barrière linguistique peut constituer un obstacle supplémentaire à la formation notamment pour les médecins francophones d'Afrique subsaharienne. L'apprentissage en ligne (e-learning) pourrait permettre de pallier à la pénurie de mentors en oncologie en Afrique francophone notamment dans le domaine des cancers gynécologiques et mammaires.

A titre d'illustration de ce paragraphe, nous avons contribué (pages suivantes) à une publication qui avait pour but de décrire une expérience d'utilisation de l'e-learning pour améliorer la formation sur le cancer du sein et du col de l'utérus en Afrique.

Nous avons rappelé que la stratégie mondiale de l'OMS sur la santé numérique indique que l'utilisation innovante des technologies de l'information et de la communication de pointe sera essentielle à la fourniture de soins de santé plus équitables. L'apprentissage en ligne peut contribuer à réduire le fardeau du cancer dans les régions éloignées et difficiles d'accès en diffusant des connaissances et des pratiques fondées sur des données probantes parmi les prestataires sans qu'ils n'aient à se déplacer de leur communauté.

Pour lever les obstacles linguistiques à l'accès à la formation en oncologie mammaire et gynécologique en Afrique, nous avons développé un programme de télé-mentorat destiné aux prestataires de soins de santé des pays francophones d'Afrique subsaharienne. Ce programme dédié aux cancers féminins a utilisé le modèle ECHO (Extension for Community Healthcare Outcome). Dans le cadre de ce programme, des vidéoconférences gratuites étaient organisées tous les derniers vendredis du mois. Depuis le lancement du programme, le nombre de participants provenant de 15 pays africains a progressivement augmenté, avec une moyenne de 30 à 35 participants par session. Une évaluation réalisée six mois après le début du programme a révélé que la plupart des participants d'ECHO ont apprécié la possibilité d'apprendre avec leurs pairs (19 sur 19), appliquaient les connaissances acquises au cours de ces sessions ECHO dans leur pratique clinique (12 sur 19), ont fait état d'une plus grande capacité à offrir des soins plus complets aux patients. La répartition limitée et inégale de la main-d'œuvre en oncologie en Afrique, peut-être être résolue en promouvant

et en améliorant les programmes de santé numérique linguistiquement appropriés. Des programmes tels que le nôtre peuvent améliorer la qualité et le niveau des soins que reçoivent les patients dans les déserts médicaux, et par conséquent contribuer à réduire les inégalités en matière de soins de santé en Afrique.

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Enhancing cervical and breast cancer training in Africa with e-learning

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Enhancing cervical and breast cancer training in Africa with e-learning



The African continent carries a high share of the global cancer burden, with cervical and breast cancers being the main drivers of cancer-related morbidity and mortality in the region.¹ Although the burden of cervical cancer has drastically decreased in high-income countries in the past three decades because of the widespread implementation of screening, early detection, human papillomavirus vaccination programmes, and improvements to accessing comprehensive cancer treatment services, nearly 90% of new cases and deaths from this preventable disease are from low-income and middle-income countries, and 19 of the 20 countries with the highest incidence rates worldwide are in Africa.² Breast cancer burden in Africa is also alarming. In the African region defined by WHO, breast cancer is the most common cancer and accounted for 16.5% of all new cancer cases in 2020.³ Women in Africa diagnosed with breast cancer have much lower survival rates, although they are generally younger than people with breast cancer in high-income settings.¹ For every 100 deaths of African women from breast cancer younger than 50 years, there are an estimated 210 new orphans,³ highlighting the societal effect of breast cancer in the region.

To urge countries to take concerted actions to tackle these global health challenges, WHO has launched two major initiatives: the Cervical Cancer Elimination Initiative in 2020⁴ and the Global Breast Cancer Elimination Initiative in 2021.⁵ In addition to the limited availability of screening, diagnostic, and treatment services, the scarcity of a well trained oncology workforce is a major impediment to the fight against cancer in Africa.⁶ As Africa faces a shortage of oncology mentors, collaborative educational initiatives with mentors and trainers within and outside the continent are essential. In July 2022, the Union for International Cancer Control organised a regional dialogue to inventory existing initiatives and identify barriers to the control of cancers that primarily affect women in francophone Africa and highlighted a shortfall of oncology training programmes in the region.⁷ At the World Cancer Congress held during October 18–20, 2022 in Geneva, Switzerland, collaborative and integrated

approaches and partnerships to optimise strategies to reduce the burden of cancers affecting women in Africa were further explored.

WHO's global strategy on digital health reports that the innovative use of cutting-edge information and communications technologies will be essential in the provision of more equitable health care,⁸ as these technology-enabled breakthroughs can increase access to services in underserved communities, including in Africa where the use of information and communications technologies is growing rapidly.⁹ In line with these WHO recommendations, a few e-learning initiatives adapted to the African context have been implemented to build the capacity of providers in oncology,¹⁰ some of which have shown promising results.¹¹ Such programmes can contribute to the reduction of the cancer burden in remote and hard-to-reach settings by spreading knowledge and evidence-based practices among providers without them having to move from their community.

Because existing e-learning programmes were mainly done in English, participation of French-speaking clinicians in Africa has been low. To address the cultural and linguistic barriers to accessing oncology training in Africa, we used our experience with establishing and maintaining effective distance-learning programmes in English, and developed a telementoring programme for French-speaking health-care providers in participating countries in Africa involved in the prevention and management of women's cancers, using the Extension for Community Healthcare Outcome (ECHO) model.¹¹ Through a collaboration with the WHO African Regional Office, stakeholders from health-care facilities, ministries of health from many francophone African countries, and Cervical and Breast Cancer Volunteer Experts from Africa, Canada, France, and the USA, in February 2022 we launched the Francophone Africa Women's Cancer ECHO—an innovative distance-learning programme in French to enhance continuing education of health-care providers in francophone African countries.

In this programme, video conferences in the form of virtual tumour boards are organised every last Friday of the month, during which providers select and present

	Agree	Neutral	Disagree
I enjoy the opportunity to learn with peers	19	0	0
The opportunity to connect with academic specialists is important to me	18	0	0
I am confident when presenting patient cases during ECHO sessions	8	10	0
The topics presented in didactics are relevant to my practice	17	2	0
The level of detail in the didactics is appropriate	18	1	0
There is enough time for questions and discussion during the ECHO sessions	14	3	2
I learn from providers who present their patient cases during ECHO sessions	18	0	0
I have applied knowledge learned in ECHO sessions to patients in my practice	12	7	0
I have adopted best practice care through my participation in ECHO sessions	11	8	0
I have developed additional clinical expertise through ECHO sessions	13	6	0
Participating in ECHO sessions is an effective way for my clinic to enhance its expertise	16	3	0
Participation in ECHO sessions increases my ability to offer more comprehensive care	17	2	0
ECHO session participation improved the coordination of care for my patients	10	8	1
I enjoy consulting with specialists about my patients' management	15	3	0

Satisfaction of the Francophone Africa Women's Cancer Project ECHO attendees based on given evaluation statements and the impact of the Francophone Africa Women's Cancer Project ECHO on the knowledge, skills, and practice of clinical providers. ECHO=Extension for Community Healthcare Outcome.

Table: Evaluation of the Francophone Africa Women's Cancer Project ECHO

clinical cases of cervical and breast pre-cancers or cancers, and receive tailored guidance from a panel of renowned experts on the diagnosis, treatment, and follow-up of patients, with an emphasis on evidence-based practices. The case-based learning (two to three clinical cases per session) is complemented by a didactic lecture given by an expert on a topic of interest to participants. These monthly ECHO sessions that last for 90 min (60 min for the case-based discussion and 30 min for the didactic lecture) are interactive, with participants providing inputs or asking questions to experts and exchanging field experience with their peers to foster the knowledge transfer process. Since the programme's inception, the total number of attendees from 15 African countries has gradually increased, averaging 30–35 participants per session. An evaluation done 6 months after the programme started found that most ECHO attendees enjoyed the opportunity to learn with their peers (19 of 19), applied knowledge gained during these ECHO sessions in their clinical practice (12 of 19), reported an increased ability to offer more comprehensive care to their patients (17 of 19), adopted best-practice care through these ECHO sessions (11 of 19), and developed additional clinical expertise (13 of 19; table).

The limited and uneven distribution of the oncology workforce in Africa, which is exacerbated by cultural and socioeconomic barriers to accessing care, can be

substantially addressed by promoting and enhancing culturally appropriate digital health programmes. Programmes such as ours can improve the quality and standard of care patients receive in underserved settings, leading to a reduction in health-care inequities in Africa.

We declare no competing interests.

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V.3. Protocole de recherche : Facteurs associés au diagnostic tardif des cancers du sein au Bénin

Introduction : Dans le monde, le cancer du sein est le premier cancer de la femme aussi bien en terme d'incidence que de mortalité et constitue un problème de santé publique (Forouzanfar et al., 2011). Bien que l'incidence en ASS soit parmi les plus faibles au Monde, la mortalité y est parmi les plus élevées témoignant d'une survie médiocre. Malgré les progrès importants réalisés à l'échelle mondiale ces dernière années dans le domaine du dépistage, 70 % des cas diagnostiqués en Afrique au Sud du Sahara le sont à des stades tardifs posant un réel problème de prise en charge thérapeutique (Pace & Shulman, 2016). Des données plus récentes au Benin montrent que plus de 65% des patientes avaient des tumeurs aux stades III ou IV (Todjinou, 2018).

Objectif : L'objectif principal de l'étude sera d'étudier les facteurs associés au diagnostic tardif des cancers du sein en milieu hospitalier à Cotonou.

Méthodes : Il s'agira d'une étude transversale et analytique avec collecte des données sur une période de 1an menée chez des patientes admises dans les centres hospitaliers de références du Bénin notamment le CNHU-HKM et le CHU-MEL pour un cancer du sein histologiquement confirmé. Les variables à étudier seront les variables sociodémographiques (âge, situation matrimoniale, niveau d'instruction, assurance maladie, zone de résidence), les variables cliniques et paracliniques (motif de consultation, délai de consultation, premier recours, premier agent de santé consulté, type histologique, grade histopronostique), les variables relatives à la connaissance et à la sensibilisation sur le cancer du sein, les variables liées à l'accès aux services de dépistage et les variables socio-culturelles liées au cancer du sein. La variable dépendante sera le stade au diagnostic avec deux modalités : précoce et tardif. Le diagnostic sera dit tardif lorsqu'il est posé à un stade évolué ou d'emblée métastatique soit stade III et IV de la classification de l'AJCC. Le diagnostic sera dit précoce lorsqu'il est posé aux stades I ou II de l'AJCC. Les données seront recueillies grâce à un questionnaire digitalisé. Une régression logistique univariée, puis multivariée sera réalisée afin d'identifier les facteurs associés au diagnostic tardif du cancer du sein. L'analyse des données sera faite avec le logiciel R. L'accord des autorités administratives compétentes des différents hôpitaux ainsi que la confidentialité sera respectée lors de l'enquête. L'avis du Comité d'Ethique de Recherche en Science de la Santé (CERSS) sera requis. Le protocole détaillé de l'étude est en **annexe 3**.

V.4. Protocole de recherche : Mutations génétiques délétères et cancer du sein au Bénin

Introduction : Le cancer du sein est le premier cancer en termes d'incidence, de prévalence et de mortalité tout sexe confondu en Afrique subsaharienne. Avec plus de 129 400 nouveaux cas en 2020, il est le premier cancer de la femme dans 27 des 48 pays d'Afrique au Sud du Sahara et la première cause de mortalité par cancer chez la femme dans 19 de ces pays (Bray et al., 2022). Il constitue donc un véritable problème de santé publique. Au Bénin, une étude réalisée sur l'âge du diagnostic des cancers du sein montre que la majorité des patientes atteintes avaient moins de 50 ans au moment du diagnostic histologique, une moyenne de 47,45ans et une tranche de 40 ans à 50 ans plus représentative (Gnangnon et al., 2020). Ce qui nous amène à suspecter des causes génétiques impliquées dans la genèse du cancer de sein chez la femme béninoise.

L'objectif principal est d'étudier les mutations génétiques délétères chez les femmes atteintes d'un cancer du sein au Bénin. De manière plus spécifique, il s'agira de mettre en place une bio-banque d'ADN sanguin et tumoral, et d'identifier les mutations constitutionnelles ou acquises impliquées dans la prédisposition au cancer du sein des femmes au Bénin.

Matériel et méthodes : Il s'agira d'une étude transversale descriptive incluant les patientes prises en charge au CNHU/HKM ou au CHU-MEL pour un cancer de sein histologiquement confirmé par examen anatomopathologique et ayant consenti à ladite étude. Les variables sociodémographiques (âge, profession, niveau d'instruction, ethnie), les caractéristiques cliniques (motif de consultation, caractéristiques de la tumeur, antécédents personnels, antécédents familiaux) le type histologique ainsi que les mutations objectivées après séquençage de l'ADN seront analysées.

Cette étude a obtenu l'approbation du Comité d'Ethique de Recherche en Sciences de Santé (CERSS) et enregistré sous le numéro N°007-2021/UAC/CERSS/P/SG/R/SA7.

L'avis éthique est en **annexe 4**.

Le protocole détaillé de l'étude est en **annexe 7**.



V.5. Protocole de recherche : La réunion de concertation pluridisciplinaire dans les hôpitaux du Bénin : état des lieux et solutions

Introduction

Le cancer est un problème majeur de santé publique à l'échelle mondiale. Bien que l'incidence de la maladie soit relativement faible en Afrique, la mortalité y est très élevée en raison du diagnostic très souvent tardif, de l'accès limité aux traitements adéquats et du non-respect des recommandations. Les réunions de concertation pluridisciplinaires (RCP) sont aujourd'hui considérées comme un pilier essentiel pour une prise en charge optimale du cancer. En effet, ces réunions ont déjà fait leur preuve dans plusieurs pays développés où plusieurs études ont montrées qu'elles favorisaient une meilleure coordination des soins, une prise de décision basée sur les preuves et une amélioration des résultats cliniques pour les patients. Cependant, peu de données sont disponibles sur l'organisation des RCP dans les pays en développement tels que le Bénin.

Objectifs

L'objectif de cette étude est de contribuer à l'amélioration de la disponibilité des RCP de cancérologie dans les hôpitaux du Bénin. Plus spécifiquement, il s'agira de :

- faire un état des lieux de la disponibilité des RCP dans les hôpitaux du Bénin,
- identifier les obstacles liés à la mise en place et à la tenue des RCP dans les hôpitaux du Bénin,
- et concevoir une solution technologique dédiée à l'organisation et la gestion des RCP dans les hôpitaux du Bénin et d'Afrique Au Sud du Sahara plus généralement.

Méthodologie

Il s'agira d'une étude transversale à visée descriptive et analytique avec collecte prospective des données. Nous ferons un premier temps un recrutement exhaustif de tous les hôpitaux publics et privés situés sur le territoire national et susceptibles de prendre en charge le cancer. Dans un second temps, nous sélectionnerons de façon aléatoire, dans chaque hôpital, un professionnel de santé parmi ceux intervenant dans les services compétents en matière de cancérologie à qui nous adresserons un questionnaire en ligne renseignant sur : la disponibilité des ressources pour le diagnostic et le traitement du cancer, l'organisation des RCP, la perception vis-à-vis des RCP et la faisabilité des RCP virtuelles. Les données issues de cette enquête en ligne serviront ensuite à la conception de la plateforme virtuelle (eRCP) qui permettra la collaboration à distance des professionnels de santé, facilitant ainsi la prise en charge multidisciplinaire des patients atteints de cancer dans le pays. Trois séances tests seront enfin organisées pour permettre aux participants d'expérimenter la plateforme dans des conditions réelles. Après chaque séance, un questionnaire nous permettra de recueillir leurs



perceptions quant à la facilité d'utilisation de la plateforme, l'utilité perçue et les suggestions d'améliorations pour satisfaire parfaitement aux besoins des professionnels de santé.

Le protocole détaillé de l'étude est en **annexe 8**.

Conclusion

Cette thèse a permis un approfondissement de la compréhension du fardeau du cancer du sein au Bénin et en Afrique au Sud du Sahara (ASS). À travers une analyse approfondie des facteurs pronostiques de cette maladie, nous avons également pu identifier des tendances significatives qui éclairent les défis auxquels sont confrontées les femmes de la région. En tant que premier cancer chez les femmes au Bénin et en ASS, avec une mortalité parmi les plus élevées au monde, le cancer du sein représente un défi majeur de santé publique nécessitant des actions urgentes.

Les résultats de cette thèse soulignent l'importance cruciale de prendre en compte les facteurs pronostiques dans l'élaboration de politiques de santé efficaces. En intégrant ces facteurs dans les programmes de détection précoce et d'accès aux soins, les décideurs politiques pourraient potentiellement réduire la mortalité liée au cancer du sein dans la région Afrique de l'OMS. En particulier, la détection précoce, l'identification des tumeurs agressives grâce à un meilleur accès à l'immunohistochimie, la mise en place de référentiels adaptés et actualisés, et un meilleur accès à la radiothérapie et aux traitements systémiques pourrait considérablement améliorer la survie des patientes.

À cet égard, il est encourageant de noter les efforts récents de l'Organisation Mondiale de la Santé (OMS) et de la Global Breast Cancer Initiative (GBCI) pour élaborer des directives mondiales sur la prise en charge du cancer du sein. Ces initiatives reconnaissent l'importance de l'accès aux soins de qualité et mettent en avant la nécessité d'une approche intégrée pour lutter contre le cancer du sein dans les contextes à ressources limitées.

Parallèlement, il est essentiel de reconnaître la nécessité de lutter contre les facteurs de risque des maladies non transmissibles (MNT) en général, et du cancer du sein en particulier, afin d'inverser la tendance actuelle d'augmentation de l'incidence du cancer du sein en Afrique au Sud du Sahara (ASS) due à l'occidentalisation des modes de vie. Des efforts visant à promouvoir une alimentation saine, à encourager l'activité physique, à réduire la consommation de tabac et d'alcool, ainsi qu'à sensibiliser à l'importance de l'auto-examen des seins et des programmes de dépistage réguliers sont essentiels pour réduire le fardeau du cancer du sein dans la région et améliorer la santé et le bien-être des femmes.

Les résultats de cette thèse pourraient être utilisés comme base pour l'élaboration de politiques et de programmes de santé publique. Les professionnels de la santé, les chercheurs et les décideurs politiques doivent travailler ensemble pour mettre en œuvre des stratégies de prévention, de dépistage et de traitement qui répondent aux besoins spécifiques des populations touchées par le cancer du sein au Bénin et en ASS.

En conclusion, cette thèse est une contribution significative dans la lutte contre le cancer du sein dans la région. En utilisant les données et les conclusions présentées ici comme guide, nous pouvons espérer progresser vers une meilleure prise en charge de cette maladie dévastatrice et améliorer ainsi la santé et le bien-être des femmes au Bénin et au-delà.

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Annexe 1: Global variation in postoperative mortality and complications after cancer surgery: a multicentre, prospective cohort study in 82 countries.

Global variation in postoperative mortality and complications after cancer surgery: a multicentre, prospective cohort study in 82 countries



GlobalSurg Collaborative and National Institute for Health Research Global Health Research Unit on Global Surgery*



Summary

Background 80% of individuals with cancer will require a surgical procedure, yet little comparative data exist on early outcomes in low-income and middle-income countries (LMICs). We compared postoperative outcomes in breast, colorectal, and gastric cancer surgery in hospitals worldwide, focusing on the effect of disease stage and complications on postoperative mortality.

Methods This was a multicentre, international prospective cohort study of consecutive adult patients undergoing surgery for primary breast, colorectal, or gastric cancer requiring a skin incision done under general or neuraxial anaesthesia. The primary outcome was death or major complication within 30 days of surgery. Multilevel logistic regression determined relationships within three-level nested models of patients within hospitals and countries. Hospital-level infrastructure effects were explored with three-way mediation analyses. This study was registered with ClinicalTrials.gov, NCT03471494.

Findings Between April 1, 2018, and Jan 31, 2019, we enrolled 15 958 patients from 428 hospitals in 82 countries (high income 9106 patients, 31 countries; upper-middle income 2721 patients, 23 countries; or lower-middle income 4131 patients, 28 countries). Patients in LMICs presented with more advanced disease compared with patients in high-income countries. 30-day mortality was higher for gastric cancer in low-income or lower-middle-income countries (adjusted odds ratio 3.72, 95% CI 1.70–8.16) and for colorectal cancer in low-income or lower-middle-income countries (4.59, 2.39–8.80) and upper-middle-income countries (2.06, 1.11–3.83). No difference in 30-day mortality was seen in breast cancer. The proportion of patients who died after a major complication was greatest in low-income or lower-middle-income countries (6.15, 3.26–11.59) and upper-middle-income countries (3.89, 2.08–7.29). Postoperative death after complications was partly explained by patient factors (60%) and partly by hospital or country (40%). The absence of consistently available postoperative care facilities was associated with seven to 10 more deaths per 100 major complications in LMICs. Cancer stage alone explained little of the early variation in mortality or postoperative complications.

Interpretation Higher levels of mortality after cancer surgery in LMICs was not fully explained by later presentation of disease. The capacity to rescue patients from surgical complications is a tangible opportunity for meaningful intervention. Early death after cancer surgery might be reduced by policies focusing on strengthening perioperative care systems to detect and intervene in common complications.

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Introduction

Cancer prevalence and its associated mortality is increasing in low-income and middle-income countries (LMICs).¹ Of the 15.2 million individuals diagnosed with cancer worldwide in 2015, 80% needed surgery.² Despite this need, fewer than 25% of people worldwide have robust access to effective surgical care.³ In tumours amenable to resection, surgery offers the best chance of cure, particularly in early-stage disease; thus, expanding the availability of surgery is likely to yield large improvements in cancer survival in LMICs.⁴

Direct estimates of the incidence and distribution of cancer by stage are absent for many LMICs, and little is

known about variation in access, quality, and outcomes in global cancer care. Breast, colorectal, and gastric cancer represent a significant burden of disease across income settings and, as such, are clear targets for intervention.^{1,2} Breast cancer is the most common cancer worldwide, and a leading cause of cancer-related morbidity and mortality in LMICs. Addressing inequities in breast cancer treatment will be essential in meeting gender equality Sustainable Development Goals, as well as health and wellbeing objectives. Colorectal cancer incidence is rising in LMICs and represents the second most common cause of cancer-related death globally. Gastric cancer is the third most common cause of

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See Online for appendix

For more on the Sustainable Development Goals see <https://www.un.org/sustainabledevelopment/sustainable-development-goals/>

Research in context**Evidence before this study**

We searched for evidence of multinational research assessing early outcomes after surgery for three globally common cancers (breast, colorectal, and gastric cancer) focusing on low-income and middle-income countries (LMICs).

We searched PubMed, MEDLINE, Google Scholar, and ClinicalTrials.gov for articles published between Jan 1, 1990, and Aug 1, 2020, using the terms "cancer" OR "malignancy" AND "surgery" AND "developing countries" OR "low income" OR "middle-income" OR "low and middle-income", without language restrictions. Identified studies largely focused on single tumour types and did not compare outcomes across different income settings. No studies systematically collected comparative data examining outcomes after cancer surgery in different income settings.

Added value of this study

To our knowledge, our study is the first to provide comprehensive data across income settings on early outcomes

in patients undergoing surgery for three common cancers. We used standardised, validated, and prospective methods to gather global, contemporaneous, and comprehensive data. Even after case-mix adjustment, patients in LMICs had higher postoperative mortality, despite similar complication rates. The capacity to rescue patients from death after the development of common postoperative complications explains a significant part of the disproportionate mortality burden in LMICs.

Implications of all the available evidence

Perioperative mortality is disproportionately greater in LMICs, which contributes to significantly worse cancer survival. Urgent assessment of pragmatic perioperative interventions led by investigators in LMICs is needed to avert avoidable mortality after the development of common complications after surgery.

cancer-related death in LMICs. These facts were reflected in a recent LMIC-led research prioritisation exercise, where cancer surgery was identified as a major priority.⁵

Irrespective of the development status of a country, surgery remains the cornerstone of cancer cure and palliation. Solid tumours are often untreated in LMICs and this carries significant macroeconomic consequences; cumulative gross domestic product losses are estimated to be as high as 1.2% for 2016–30.⁶ Cancer resection procedures are often highly invasive, leading to postoperative morbidity and mortality. In previous work, we identified significant global disparities in surgical outcomes, with patients in LMICs two to three times more likely to sustain a major complication or to die after surgery.^{7,8} These consequences are devastating for patients and their families and, in the context of cancer treatment, complications can lead to long-term morbidity or death, increased treatment costs, and delays in adjuvant treatment. Rescuing patients who sustain a major complication from dying has become an important focus of quality improvement in surgery.⁹ Not only must complications be minimised, but the timely recognition and management of complications is essential if avoidable mortality is to be minimised. Little is known about factors contributing to early death and complications after cancer surgery in LMICs.

This insufficiency of high-quality data limits global efforts to improve cancer care. Strategic planning mandates detailed and accurate information, so that appropriate resources can be allocated and quality improvement prioritised. Demographic and clinical data, together with details of hospital resources, are needed to help refine public health initiatives, treatment strategies, and quality improvement interventions. To address these

issues, we did an international, multicentre, prospective cohort study that aimed to determine the variation in mortality and complication rates for breast, colorectal, and gastric cancers in low-income, middle-income, and high-income countries.

Methods**Study design and setting**

This international, multicentre, prospective cohort study was done according to a published protocol.¹⁰ The study was designed in a collaborative research prioritisation workshop.⁵ Breast, colorectal, and gastric cancers were prioritised on the basis of global prevalence and mortality, and relevance to the majority of our collaborators, who are predominantly general surgeons and manage these cancers regularly. To maximise case ascertainment, ensure data quality, and enable engagement across a global network, a pragmatic decision was taken not to collect data on additional cancer types. All Global Surgery study documents, training materials, and language translations are available online. Teams of local investigators undertook the study and were coordinated by a network of national lead investigators. The collaborative network method has been described in detail previously.^{7,8} Any health-care facility providing emergency or elective surgery for breast, colorectal, or gastric colorectal cancer worldwide was eligible to participate.

A UK National Health Service (NHS) Research Ethics proportionate review considered this study exempt from formal research registration (South East Scotland Research Ethics Service, reference NR/161AB6) because it was deemed a clinical audit. Individual centres obtained their own audit or institutional approval, together with ethical approval as per local regulations.

For more on the Global Surgery resources see globalsurg.org/g53

Participants

Investigators included consecutive patients undergoing surgery for breast, colorectal, or gastric cancer, from one or more 28-day period between April 1, 2018, and Jan 31, 2019, with validation performed until April 23, 2019. Inclusion criteria were adult patients aged 18 years or older; undergoing their first surgical procedure for the treatment of one of the three cancers; and requiring a skin incision performed under general or neuraxial (eg, regional, epidural or spinal) anaesthesia. All patients fulfilling the inclusion criteria within the defined period were enrolled. A 28-day period was chosen to balance sample size requirements and pragmatism for the working clinicians who were enrolling patients and contributing data.

The inclusion of primary breast, colorectal, and gastric cancer was based on global prevalence, potential for cure with surgical treatment, and relevance to general surgeons working in resource-constrained settings. There was an absolute requirement for all cases in the chosen period to be included, but no minimum number was set to avoid bias against smaller centres. Patients provided consent to participate if required by local research regulations and could withdraw at any time during the study period. Due to potential limitations in preoperative diagnosis in some settings, all patients receiving surgical treatment for suspected cancer were enrolled. Patients subsequently found to have a non-oncological diagnosis were excluded from data analysis. Emergency procedures were defined as unplanned, non-elective operations. Open and minimally invasive procedures (eg, laparoscopic or robotic) were eligible. Patients were excluded if the primary pathology was not suspected to be breast, colorectal, or gastric cancer; if the pathology was a suspected cancer recurrence; or if they were undergoing a procedure that did not require a skin incision.

Data collection and validation

Data variables were selected to be objective, standardised, easily transcribed, and internationally relevant to maximise completeness and accuracy. Local investigators uploaded records to a secure website, provided using the Research Electronic Data Capture system.¹¹ The lead investigator at each site checked the accuracy of all cases before data submission. To ensure data quality, real-time assessment was done on entry into the database and disparities highlighted to the local collaborator for immediate review. The submitted data were then checked centrally and when missing data were identified, the local lead investigator was contacted and asked to complete the record. Online data visualisation tools aided this process. Once vetted, the record was accepted into the dataset for analysis. Records that were vetted but remained incomplete were included in the patient flow chart, but excluded from analysis.

Patient variables included age, sex, performance status according to the Eastern Cooperative Oncology Group,

physical status according to the American Society of Anesthesiologists (ASA) grading system, and smoking status. Disease-related variables included cancer type, disease stage, timing of surgery (elective vs emergency), intent of surgery (curative vs palliative), and use of WHO surgical checklist. Presence of preoperative perforation or obstruction, and operative approach (open or minimally invasive) were also included for gastric and colorectal cancers.

Disease stage was defined according to the Essential TNM classification of malignant tumours system,¹² to account for differences in local protocols and availability of investigations for preoperative staging. A pragmatic view was taken to the confirmation of cancer diagnosis, because postoperative pathological examination worldwide is dependent on the availability of patient and health-care resources. To reflect this situation, we recorded the basis of cancer diagnosis using a hierarchical scale ranging from clinical diagnosis only to pathological confirmation (appendix p 7).

Data validation was done in three parts across a representative sample of centres, according to a prespecified protocol (appendix pp 47–51). First, centres self-reported the key processes used to identify and follow up patients (appendix p 7). Second, independent validators (ie, doctors, nurses, or medical students who were not part of the recruiting teams) quantitatively reported case ascertainment and sampled data accuracy. Third, validators identified any missing eligible patient within the local cohort and collected the missing information

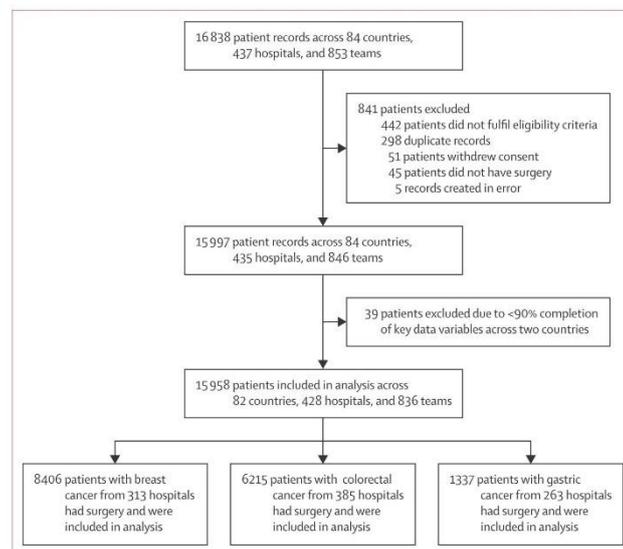


Figure 1: Patient flow chart

for each omission (age, sex, operation urgency, and 30-day mortality). These data were used to determine whether patient data were missing at random.

	High (n=9106)	Upper-middle (n=2721)	Low and lower- middle (n=4131)	Total (N=15958)
Cancer type				
Breast	4220 (46.3%)	1319 (48.5%)	2867 (69.4%)	8406 (52.7%)
Colorectal (colon or rectum)	4174 (45.8%)	1113 (40.9%)	928 (22.5%)	6215 (38.9%)
Gastric	712 (7.8%)	289 (10.6%)	336 (8.1%)	1337 (8.4%)
Age, years	65.0 (13.4)	58.0 (13.6)	51.9 (12.7)	60.4 (14.4)
Sex				
Male	2864 (31.5%)	791 (29.1%)	723 (17.5%)	4378 (27.4%)
Female	6231 (68.4%)	1928 (70.9%)	3406 (82.4%)	11565 (72.5%)
Missing	11 (0.1%)	2 (0.1%)	2 (0%)	15 (0.1%)
ASA grade				
I	1148 (12.6%)	739 (27.2%)	1285 (31.1%)	3172 (19.9%)
II	4769 (52.4%)	1474 (54.2%)	2242 (54.3%)	8485 (53.2%)
III	2558 (28.1%)	391 (14.4%)	412 (10.0%)	3361 (21.1%)
IV	217 (2.4%)	42 (1.5%)	36 (0.9%)	295 (1.8%)
V	17 (0.2%)	1 (0%)	10 (0.2%)	28 (0.2%)
Missing	397 (4.4%)	74 (2.7%)	146 (3.5%)	617 (3.9%)
Body-mass index				
<18.5	231 (2.5%)	111 (4.1%)	234 (5.7%)	576 (3.6%)
18.5-24.9	3267 (35.9%)	1148 (42.2%)	1511 (36.6%)	5926 (37.1%)
25-30	3079 (33.8%)	882 (32.4%)	1354 (32.8%)	5315 (33.3%)
>30	1773 (19.5%)	470 (17.3%)	867 (21.0%)	3110 (19.5%)
Missing	756 (8.3%)	110 (4.0%)	165 (4.0%)	1031 (6.5%)
>10% weight loss				
No	6560 (72.0%)	1813 (66.6%)	2896 (70.1%)	11269 (70.6%)
Yes	1049 (11.5%)	673 (24.7%)	917 (22.2%)	2639 (16.5%)
Missing	1497 (16.4%)	235 (8.6%)	318 (7.7%)	2050 (12.8%)
ECOG performance status				
0	5090 (55.9%)	1732 (63.7%)	2136 (51.7%)	8958 (56.1%)
1	2152 (23.6%)	639 (23.5%)	1085 (26.3%)	3876 (24.3%)
2	961 (10.6%)	201 (7.4%)	570 (13.8%)	1732 (10.9%)
3	299 (3.3%)	94 (3.5%)	176 (4.3%)	569 (3.6%)
4	32 (0.4%)	9 (0.3%)	31 (0.8%)	72 (0.5%)
Missing	572 (6.3%)	46 (1.7%)	133 (3.2%)	751 (4.7%)
Smoking				
No, never	5363 (58.9%)	1902 (69.9%)	3631 (87.9%)	10896 (68.3%)
Stopped >6 weeks ago	1650 (18.1%)	322 (11.8%)	181 (4.4%)	2153 (13.5%)
Yes, current smoker	1174 (12.9%)	347 (12.8%)	170 (4.1%)	1691 (10.6%)
Missing	919 (10.1%)	150 (5.5%)	149 (3.6%)	1218 (7.6%)
Diabetes				
No	7594 (83.4%)	2179 (80.1%)	3100 (75.0%)	12873 (80.7%)
Diet controlled	209 (2.3%)	42 (1.5%)	45 (1.1%)	296 (1.9%)
Medication controlled, non-insulin	895 (9.8%)	324 (11.9%)	422 (10.2%)	1641 (10.3%)
Insulin dependent	279 (3.1%)	120 (4.4%)	191 (4.6%)	590 (3.7%)
Missing	129 (1.4%)	56 (2.1%)	373 (9.0%)	558 (3.5%)

(Table continues on next page)

Outcomes

The primary outcome measures were 30-day mortality and 30-day major complication, as defined by Clavien-Dindo grade III, IV, or V.¹³ Death was included in the definition of major complication and therefore was not a competing risk. Capacity to rescue was defined as the absolute risk difference of death in patients sustaining a complication of surgery. Mortality conditional on major complication was analysed post hoc.

The secondary outcome measures were defined in the protocol¹⁰ and designed to describe cancer care quality. They included: 30-day any complication (defined by Clavien-Dindo grade I-V); 30-day unplanned reoperation (defined as operative, radiological, or endoscopic reoperation any time until 30 days after surgery); unplanned readmission to a health-care facility; cancer-specific complications including seroma (breast), anastomotic leak (gastric and colorectal), surgical site infection (all),⁸ abscess formation (all), and postoperative bleed (all); cancer treatment pathways; and hospital-level care processes. Patients were assessed at 30 days to determine postoperative outcomes, with follow-up done in person, by telephone, or by review of medical or re-admission records, dependent on local practices.

Sample size

As described in the protocol,¹⁰ consideration was given to the sample size needed to compare income groups. Estimates of 30-day mortality for gastrointestinal cancer surgery were determined using data from the GlobalSurg 1 and 2 studies.^{7,8} Stratification of results by country income group show differences between high-income countries and LMICs in both emergency surgery (75 [11.6%] of 644 vs 59 [27.3%] of 216, respectively) and elective surgery (30 [2.0%] of 1501 vs 23 [5.5%] of 416, respectively). An indicative sample size calculation using the smaller of these estimates suggests around 500 patients per group at 80% power (2.0% vs 5.5%, $\alpha=0.05$) or 640 patients per group at 90% power would be required to conclude a difference in 30-day mortality rate between income groups.

Statistical analysis

Variation across different international health settings was assessed by stratifying countries by World Bank country group classifications. Differences between World Bank tertiles were tested with the Pearson χ^2 test for categorical variables and with the Kruskal-Wallis test for continuous variables. Multilevel logistic regression models were constructed to account for case mix (differing patient, disease, and operative characteristics), with population stratification by hospital and country of residence incorporated as random intercepts with constrained gradients. Further post hoc analyses were then performed exploring the relationship between primary outcome measures, patient factors, and hospital care facilities.

Models were constructed using the following principles: variables associated with outcome measures

in previous studies were accounted for; demographic variables were included in model exploration; population stratification by hospital and country of residence was incorporated as random effects; all first-order interactions were checked and included in final models if found to be influential (reaching statistical significance or resulting in a 10% or greater change in the odds ratio (OR) of the explanatory variable of interest); final model selection was done using a criterion-based approach by minimising the Akaike information criterion and discrimination determined using the C-statistic (area under the receiver operator curve). Effect estimates are presented as ORs and 95% CIs. The variance explained at each level of multilevel models was determined.¹⁴ The conditional pseudo R² was defined as the sum of the variance components of fixed and all random effects divided by total variance. The variance explained by each component (marginal pseudo R²) was expressed as a proportion of the conditional pseudo R².

Mediation analysis was performed by three-way decomposition of total effects into direct, indirect, and interactive effects.¹⁵ The mediators examined were at the level of the hospital, defined as the presence or absence of postoperative care infrastructure, and it was assumed that there was no causal relationship between these and patient-level covariates. Similarly, no mediator-outcome confounders were specified. Uncertainty was determined using bootstrap resampling (5000 draws) and CIs constructed using percentiles.

Quantities of interest were calculated from logistic regression models for different covariate levels (patient and disease characteristics). Absolute risk differences were calculated, and CIs determined using bootstrap resampling. The number needed to treat to benefit was defined as the reciprocal of the absolute risk difference.

All analyses were done using R (version 3.6.3), using the finalfit, tidyverse, and lme4.

This trial was prospectively registered with ClinicalTrials.gov, NCT03471494.

Role of the funding source

National Institute for Health Research (NIHR) Global Health Research Unit Grant (NIHR 17-0799) funded hub development in a subset of contributing countries. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the UK Department of Health and Social Care. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the Article. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between April 1, 2018, and Jan 31, 2019, 16 838 patient records were submitted for analysis. 880 (5.2%) did not fulfil the inclusion criteria, leaving 15 958 records for

	High (n=9106)	Upper-middle (n=2721)	Low and lower- middle (n=4131)	Total (N=15 958)
(Continued from previous page)				
HIV tested				
No	8650 (95.0%)	1626 (59.8%)	2118 (51.3%)	12394 (77.7%)
Yes, negative	404 (4.4%)	1067 (39.2%)	2001 (48.4%)	3472 (21.8%)
Yes, positive	9 (0.1%)	26 (1.0%)	12 (0.3%)	47 (0.3%)
Missing	43 (0.5%)	2 (0.1%)	0	45 (0.3%)
Distance from hospital to home, km				
<10	3497 (38.4%)	677 (24.9%)	575 (13.9%)	4749 (29.8%)
10 to 19.9	1798 (19.7%)	617 (22.7%)	673 (16.3%)	3088 (19.4%)
20 to 49.9	1756 (19.3%)	479 (17.6%)	768 (18.6%)	3003 (18.8%)
50 to 100	738 (8.1%)	195 (7.2%)	514 (12.4%)	1447 (9.1%)
>100	576 (6.3%)	439 (16.1%)	1409 (34.1%)	2424 (15.2%)
Missing	741 (8.1%)	314 (11.5%)	192 (4.6%)	1247 (7.8%)

Numbers are n (%) or mean (SD). High income included 31 countries and 241 hospitals. Upper-middle income included 23 countries and 81 hospitals. Lower-middle income or low income included 28 countries and 106 hospitals. The total column therefore includes 82 countries and 428 hospitals. For patient characteristics by cancer type, see appendix p 2. ASA=American Society of Anesthesiologists. ECOG=Eastern Cooperative Oncology Group.

Table: Patient characteristics by country income group

the final analysis (figure 1). These patients were from 428 hospitals, across 82 countries—22 in Africa, 17 in Asia, 30 in Europe, five in North America, two in Oceania, and six in South America.

On stratification by World Bank country income groups, 9106 (57.1%) patients were from high-income countries, 2721 (17.0%) from upper-middle-income countries, and 4131 (25.9%) from low-income or lower-middle-income countries (table; appendix p 2). Patients from upper-middle-income countries and low-income or lower-middle-income countries were younger, more likely to have lost weight, and had fewer comorbidities compared with patients from high-income countries. Missingness was low and no patterns were seen when comparing included and missing data (appendix pp 2–3).

Overall, 8406 (52.7%) patients had surgery for breast cancer, 6215 (38.9%) for colorectal cancer, and 1337 (8.4%) for gastric cancer (figure 1). The distribution of cancer type, unadjusted mortality, and complication rates across country income group are shown in figure 2.

The proportion of patients with later-stage disease who had surgery was greater in upper-middle-income countries and low-income or lower-middle-income countries for all three cancer groups (figure 3; appendix p 8). There was a strong positive correlation between cancer stage and performance status for patients with gastric cancer, and a weaker relationship in patients with breast and colorectal cancer (appendix pp 9–14). No strong relationship between operative risk (ASA grade) and cancer stage was seen.

30-day mortality was higher for gastric cancer in the low-income or lower-middle-income group (33 [10.1%] of 326) and for colorectal cancer in the upper-middle-income group (47 [4.3%] of 1102) and low-income or lower-middle-income group (63 [7.0%] of 905),

	Breast cancer	Colorectal cancer	Gastric cancer
Overall	8406 patients with breast cancer from 313 hospitals Mortality 16 (0.2%) of 8334 Major complication 496 (5.9%) of 8366 Any complication 3024 (36.1%) of 8366	6215 patients with colorectal cancer from 385 hospitals Mortality 204 (3.3%) of 6149 Major complication 889 (14.4%) of 6181 Any complication 2934 (47.4%) of 6187	1337 patients with gastric cancer from 263 hospitals Mortality 71 (5.4%) of 1311 Major complication 192 (14.5%) of 1321 Any complication 612 (46.3%) of 1321
High income	4220 patients from 156 hospitals Mortality 4 (0.1%) of 4207 Major complication 218 (5.2%) of 4215 Any complication 1346 (31.9%) of 4215	4174 patients from 225 hospitals Mortality 94 (2.3%) of 4142 Major complication 590 (14.2%) of 4162 Any complication 1977 (47.5%) of 4165	712 patients from 147 hospitals Mortality 27 (3.8%) of 702 Major complication 105 (14.8%) of 709 Any complication 311 (43.9%) of 709
Upper-middle income	1319 patients from 64 hospitals Mortality 2 (0.2%) of 1295 Major complication 61 (4.7%) of 1306 Any complication 477 (36.5%) of 1306	1113 patients from 71 hospitals Mortality 47 (4.3%) of 1102 Major complication 125 (11.3%) of 1107 Any complication 449 (40.5%) of 1109	289 patients from 44 hospitals Mortality 11 (3.9%) of 283 Major complication 26 (9.2%) of 284 Any complication 142 (50.0%) of 284
Low or lower-middle income	2867 patients from 93 hospitals Mortality 10 (0.4%) of 2832 Major complication 217 (7.6%) of 2845 Any complication 1201 (42.2%) of 2845	928 patients from 89 hospitals Mortality 63 (7.0%) of 905 Major complication 174 (19.1%) of 912 Any complication 508 (55.6%) of 913	336 patients from 72 hospitals Mortality 33 (10.1%) of 326 Major complication 61 (18.6%) of 328 Any complication 159 (48.5%) of 328

Figure 2: Patients and outcomes by cancer type and country income group

Data are for 15 958 patients from 82 countries and 428 hospitals. Crude outcome rates are shown for 30-day mortality, 30-day major complication (Clavien-Dindo grade \geq III), and 30-day any complication.

compared with the high-income group (gastric 27 [3.8%] of 702; colorectal 94 [2.3%] of 4142; figure 3; appendix p 20). However, the proportion of patients with a major complication or any complication was similar across all income groups.

Outcomes were adjusted in three-level models accounting for patient and disease factors nested within hospitals and country of treatment (figure 4; appendix pp 22–38). Higher 30-day mortality was seen in gastric cancer in low-income or lower-middle-income countries (adjusted OR [aOR] 3.72, 95% CI 1.70–8.16) and in colorectal cancer in upper-middle-income countries (2.06, 1.11–3.83) and low-income or lower-middle-income countries (4.59, 2.39–8.80; figure 4). No difference in mortality was seen in breast cancer.

The proportion of patients sustaining a major complication or any complication in these adjusted analyses was similar across country income groups, with weak evidence of fewer major complications after breast surgery in the upper-middle-income group (figure 4).

No statistical interactions were seen between patient factors and country income group for mortality or complications; for example, the effect of age, body-mass index, and ASA grade on outcomes did not differ by country income group.

Given similar complication rates across country income groups, we did an analysis defined post hoc to examine factors predicting mortality after major complications in colorectal and gastric cancer, to determine where capacities to rescue patients might exist.

The proportion of patients sustaining a major complication who subsequently died was higher in upper-middle-income and low-income or lower-middle-income countries compared with high-income countries, in both unadjusted (figure 3) and adjusted analyses

(appendix p 4). The relationship between mortality and country income group was consistent across cancer stage of presentation, except for stage IV gastric cancer, where mortality was high across all country income groups (appendix p 4). Similarly, the proportion of patients sustaining complications across country income groups was unchanged after stratification by stage of presentation (appendix p 4).

The pattern of complications occurring within cancer types was broadly similar across country income groups (appendix p 5). No systematic differences in the types of complications being sustained (eg, bleeding, infection) were seen in different country income groups.

In a model accounting for patient factors and clustering by country and hospital, patients in upper-middle-income (aOR 3.89, 2.08–7.29) and low-income or lower-middle-income (6.15, 3.26–11.59) groups were more likely to die after a major complication compared with the high-income group (figure 5; appendix p 43). Patient performance status and emergency surgery were strong predictors of death after major complication. Although patients with stage IV cancer had a greater probability of dying after major complication, stage I to III cancer was not associated with an excess mortality when accounting for other variables in the model. A sensitivity analysis using final pathological staging, as opposed to preoperative clinical staging, showed similar findings (appendix pp 15–16).

In a four-level model of patients nested in hospitals, countries, and World Bank income groups, 60% of the variation in outcome captured by the model (pseudo R^2 0.42) was explained by patient or disease factors, with the remaining 40% explained by hospital, country, and country income group factors.

We assessed hospital facilities and processes to determine relationships with excess mortality after

major complications. Hospitals in high-income (n=232), upper-middle-income (n=72) and low-income or lower-middle-income (n=95) groups were sampled. Hospitals in upper-middle-income and low-income or lower-middle-income groups were less likely to have postoperative care infrastructure (designated postoperative recovery areas, consistently available critical care facilities, and an available and working CT) and cancer care pathways (tumour board, oncology services, and palliative care services; appendix pp 41–42).

The association between country income group and 30-day mortality was examined in a three-way decomposition mediation model of postoperative care infrastructure (figure 5; appendix p 44). No interaction was found between this mediator and country income group. A significant proportion of the excess mortality after major complication was mediated by the absence of postoperative care infrastructure in low-income or lower-middle-income (aOR 1.19, 95% CI 1.01–1.42; 20%) and upper-middle-income (1.19, 1.01–1.42; 22%) groups. The absolute risk differences for 30-day mortality after major complication with and without consistently available postoperative care infrastructure were examined for common patient covariates (figure 5; appendix p 45). The presence of postoperative care infrastructure was associated with fewer deaths in both the low-income or lower-middle-income group (seven to ten fewer deaths per 100 major complications, number needed to treat 10–14) and the upper-middle-income group (five to eight fewer deaths per 100 major complications, number needed to treat 13–20). Cancer care pathways were not shown to mediate any association with 30-day mortality.

In 265 hospitals in 69 countries randomly selected for validation (1060 hospital-weeks of data collection), 3805 patients fulfilled inclusion criteria compared with 3669 (96.4%) in the primary dataset (appendix p 47). Accuracy was high for the validated continuous predictor (Pearson's correlation coefficient 0.99; appendix p 50). Agreement for categorical predictors was good (sex, T stage, urgency, and intent; Cohen's κ coefficients >0.75; appendix p 51) and lower for N stage (κ 0.67). Agreement was very good for 30-day mortality (κ 0.89) and good for 30-day major complication (κ 0.63).

Discussion

Differences in early cancer outcomes in LMICs compared with high-income countries are often attributed to the advanced stage of presentation, together with an absence of access to cancer-specific treatments. In this prospective, international cohort study of 15 958 patients in 82 countries undergoing surgery for breast, colorectal, and gastric cancer, we show that 30-day postoperative mortality is four-times higher in resource-limited settings, despite patients experiencing similar major complication rates. Although patient factors partially explained the higher

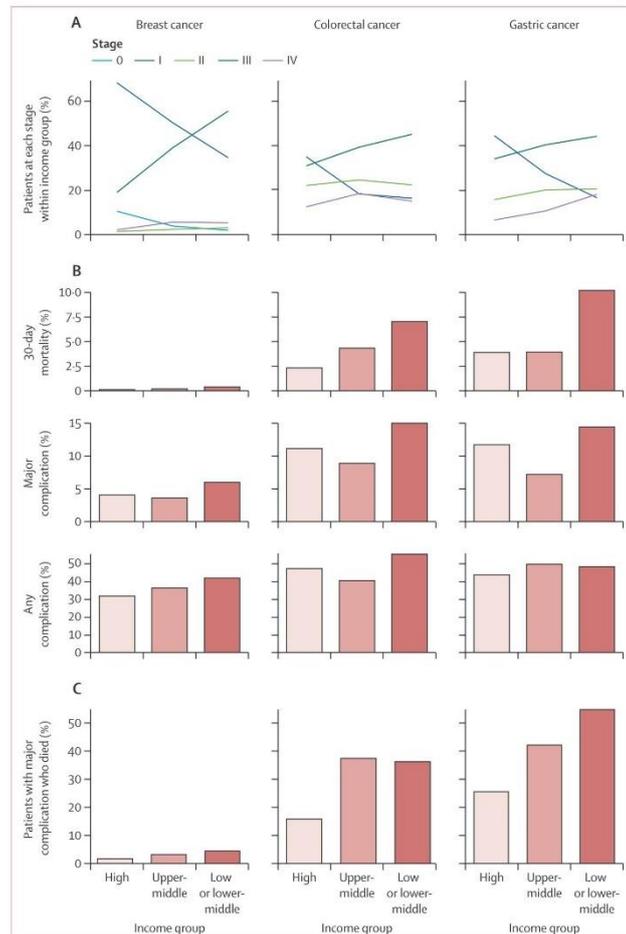


Figure 3: Stage of presentation (A), 30-day mortality (B), and 30-day complications (C) by cancer and country income group

(A) Proportion of patients enrolled by cancer stage by country income group. (B) Proportion of patients dying or sustaining a major complication or any complication by day 30 after surgery stratified by country income group. (C) Proportion of patients sustaining a major complication who died within 30 days.

postoperative mortality rate in LMICs, health system factors, including access to postoperative monitoring, emergent imaging, and critical care facilities also appeared key, resulting in an insufficiency of capacity to rescue after major complications. This excess mortality after cancer surgery will hamper cancer control efforts in LMICs, and prevent cancer patients, communities, and economies from realising the benefits of cancer-specific treatments.

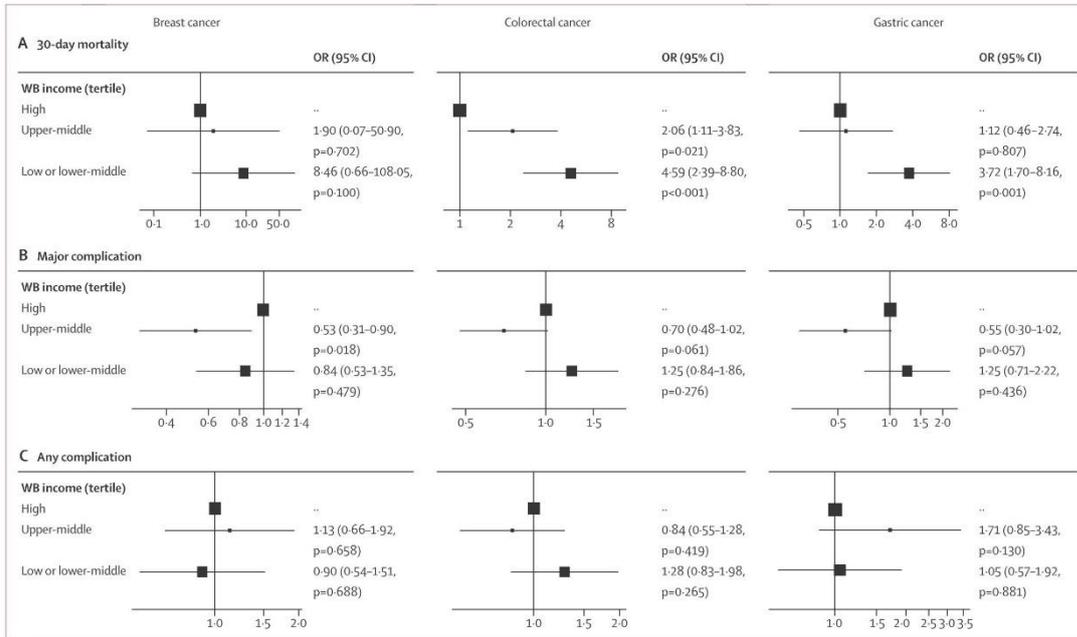


Figure 4: Multilevel logistic regression-adjusted outcomes by World Bank country income group
 Models were built incorporating patient and disease factors specific to each cancer. Univariable, full multivariable, parsimonious multivariable, and multilevel (patient, hospital, country) models for each outcome in each cancer type are given in the appendix (pp 22–38). Box size proportional to group size (n). WB=World Bank. OR=odds ratio.

For more on the Global Cancer Observatory see <https://gco.iarc.fr/>

According to Global Cancer Observatory data, cancer is a leading cause of death and disability worldwide, exerting substantial economic effects in countries at all stages of development,¹⁶ with a disproportionate burden of disease now emerging in LMICs.² Surgery is fundamental to the treatment of solid cancers across all income settings, acting as a pivotal component of multidisciplinary care, together with imaging, pathology, chemoradiotherapy, and palliation. Effective surgical care plays a crucial role in the prevention of death from cancer,² and requires systems of the highest quality throughout the preoperative and postoperative periods.³ If the opportunity to strengthen surgical cancer systems is not taken, an estimated US\$6.2 trillion in gross domestic product will be lost by 2030.²

Mortality reported in our study across LMICs for both gastric (7.2%) and colorectal (5.5%) cancer were higher than current global estimates.¹⁷ Existing perioperative mortality rates in the literature are limited by the absence of standardised reporting and risk stratification, and are often derived from small, single-centre studies. The 30-day mortality in our study was similar to that in our previous multicentre observational cohorts.²⁸ Across gastric and colorectal cancers, variation in 30-day mortality between

high-income countries and LMICs was shown after both emergency (7.1% vs 18.0%, respectively) and elective (1.9 vs 4.0%, respectively) surgery.

There are well described factors that could contribute to an early excess mortality after cancer surgery. Locally advanced or metastatic cancer is a common initial presentation in LMICs, due in part to reduced access to timely and affordable surgical services.² Delays in presentation result in poorer survival through a combination of cancer progression,¹⁸ cancer-related cachexia,¹⁹ and the consequences of emergency presentation. Achieving early detection and treatment through cancer screening initiatives is important, and often the focus of public health initiatives and funding.²⁰ However, in this study we show that excess mortality after cancer surgery in LMICs is only partly explained by the later presentation of disease. We have shown an excess in postoperative mortality despite similar rates and patterns of complications. The importance of rescuing patients from common complications is now well established with variation described globally.²¹ To our knowledge, our study is the first to identify capacity to rescue as an important early determinant of outcomes from cancer surgery in resource-restricted

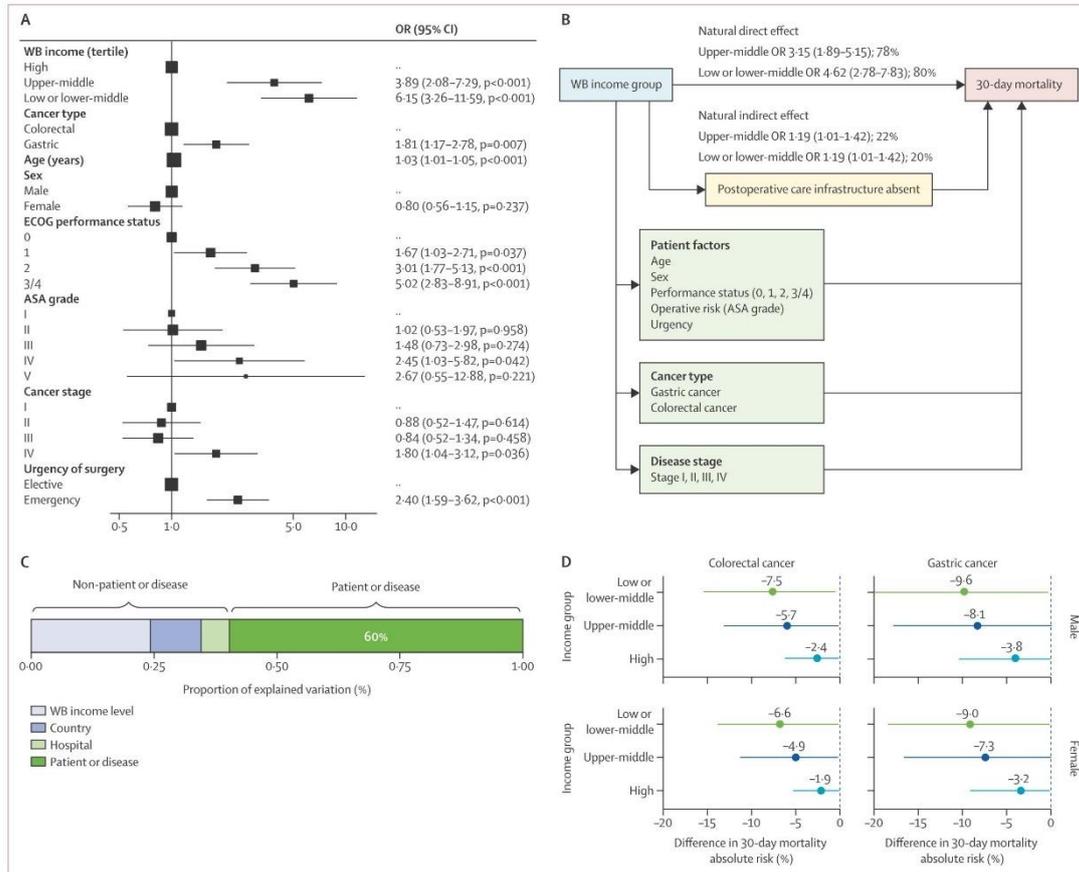


Figure 5: Capacity to rescue from major complication
 (A) Multilevel logistic regression model for predictors of death after major complication in colorectal and gastric cancer. Box size proportional to group size (n). (B) Three-way decomposition mediation model of the proportion of the effect of country income group on 30-day mortality mediated by postoperative care infrastructure (the consistent presence of a designated postoperative recovery area, the availability of critical care facilities, and the existence of a working CT scanner). (C) Proportion of 30-day mortality variation explained at the level of patient or disease, hospital, country, and country income group, in patients with colorectal or gastric cancer who died after major complication. The variance explained at each of the four levels of the model (marginal pseudo R²) is expressed as a proportion of the total variance explained (conditional pseudo R²). (D) Absolute risk difference for 30-day mortality after major complication in the presence of consistently available postoperative care infrastructure. Estimates for age 55 years, ECOG performance status 1, ASA grade 2, cancer stage II, and elective surgery. WB=World Bank. OR=odds ratio. ECOG=Eastern Cooperative Oncology Group. ASA=American Society of Anesthesiologists.

settings. Furthermore, we have shown an association between the consistent presence of postoperative care infrastructure and lower mortality rates after major complications. The capacity to rescue patients is likely to limit expected reductions in mortality from current global development funds and multilateral investments in cancer control. Better perioperative care systems to detect and intervene in common complications are essential if early death after cancer surgery is to be reduced.

A major strength of this study is its prospective design and deep patient-level and hospital-level data collected simultaneously from a wide breadth of global settings. More than 100 variables were included, making it one of the richest datasets in this area, to our knowledge. The use of the Essential TNM system, together with standard TNM 8 classifications, make meaningful comparisons of cancer stage possible in settings with limited access to imaging and pathological services.¹² The assessment of cancer stage, treatment, and outcome was standardised,

and training provided through an online platform. Data quality was ensured through collaborator-facing web applications and real-time data entry quality assurance. An independent validation study verified data accuracy and case ascertainment. Quantification of surgical cancer care in resource-limited settings has been hindered by an insufficient amount of high-quality data.^{4,17,22} This study therefore contributes to closing this knowledge gap and allows meaningful comparison from multiple income settings with accurate case-mix adjustment.

Limitations of this study include looking at outcomes only in the 30 days after surgery. Oncological outcomes are essential in capturing the effectiveness of cancer treatments, including surgery, and these outcomes are poorly captured and understood in resource-limited settings.²⁴ Disease-free and overall survival after surgery are likely to be significantly lower in LMICs, for many of the reasons described in this study, including the later stage disease across included cancers. The effect of delayed surgery in life-years lost for stage I–III disease is well described in high-income countries;²³ however the impact of this in global settings is less clear. The current study will be extended to capture longer-term outcomes and other cancers in the future, which should add significantly to the picture of global surgical cancer care we have provided here.

Only patients undergoing primary surgery for breast, colorectal, or gastric cancers were included in our study, and therefore outcomes in patients receiving non-surgical care were not examined. Furthermore, the relationship between outcomes and hospital-level facilities were associations. Hospitals with CT and critical care facilities are likely to have other differences in infrastructure and processes that might contribute to better outcomes. Although we provide several important measures of hospital facilities (appendix pp 41–42), further detailed analyses of these data are ongoing. Finally, the substantial economic and financial costs to patients undergoing cancer treatment are known to be significant, but were not measured.

Reducing early mortality after surgery is key to improving cancer outcomes and achieving Universal Health Coverage for non-communicable diseases worldwide. The Lancet Commission on Global Cancer Surgery identified the key requirements to scale up surgical cancer services by 2030.³ Improvements in the provision of cancer care remain essential if Sustainable Development Goals are to be met. Yet, detailed global information supporting focused initiatives to develop infrastructure, improve quality, and implement effective interventions remains limited. Although complete analysis of the patient pathway was not possible within this study, we identified multiple components of the surgical health system and patient-level risk factors that could be targeted for further study and intervention. High-quality perioperative care requires appropriate

recovery and ward space, a sufficient number of well trained staff, the use of early warning systems, and ready access to imaging, operating theatre space, and critical care facilities to deal with complications when they occur—the delivery of which is even more challenging in the present COVID-19 pandemic.²⁴

Access to cancer surgery is an important barrier to safe and effective care for people with cancer in LMICs.²⁵ Improved access comes with further opportunities for optimisation of individual patients through, for instance, nutritional interventions and neoadjuvant therapies. Addressing these factors with high-quality interventional trials to build a global evidence base for the delivery of safe cancer surgery is likely to have significant effect and improve cancer survival.

This study has produced a unique prospective dataset of patients undergoing breast, colorectal, and gastric cancer surgery worldwide. Future research should focus on the detailed characterisation of perioperative care processes and the implementation of strategies to both reduce complication rates, and to rescue patients from complications when they do occur. Policy makers worldwide must balance investments in the early detection and treatment of cancer with the simultaneous improvement in safe perioperative care. Without these investments, mortality gains in cancer control will not be fully realised.

Contributors

Study design, data collection, data analysis, data interpretation, and writing (SRK, MLAA, EMH, PB, JEF, MivBH, KAM, FP, ARM, NJS, ST, HST, and TGW); study design, data collection, and writing (AOAdi and SWA-S); study design, data interpretation, and writing (AOAdi, TMD, JCAI, TPK, RJJ, and DM); data collection, data interpretation, and writing (ISA-S, AJD, FN, and TDP); study design, data collection, data interpretation, and writing (AB, KMC, AC-C, JG, MCML, IL, and DN); study design and writing (BMB); data collection, data interpretation, writing, and revision (ME and BL); study design, data collection, and data interpretation (CJF and RTS); data analysis, data interpretation, and writing (DNG); study design and data interpretation (JM, HKS); data collection (RLM); data analysis and data interpretation (LN and AMR); study design, data analysis, data interpretation, and writing (RP and CAS); study design, data collection, and Article revisions (AUQ); data interpretation and writing (JS); data interpretation, writing, and critical review (MAW); data collection and manuscript revisions (JW); and data verification (EMH, SRK, CAS, RP, TMD, and LN).

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Declaration of interests

MivBH reports personal fees from Mylan, Alesi Surgical, Johnson and Johnson, and Medtronic; grants and non-financial support from Stryker; and grants from Olympus, outside the submitted work. All fees were paid to MivBH's employing institution. PB reports grants and personal fees from the Medical Research Council (MRC); grants from MRC, National Institute for Health Research Health Technology Assessment, and Wellcome Trust; and personal fees from AG Biotest, outside the submitted work. TPK reports personal fees from Olympus Surgical outside the submitted work. All other authors declare no competing interests.

Data sharing

The dataset can be explored using an online visualisation application online. Hospital-level data can be shared by application to the corresponding author. For analyses of patient-level identifiable data within our trusted research environment, please contact the corresponding author.

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For more on the dataset see cancer.globalsurg.org

Annexe 2 : Cancer incidence estimates in adults aged 60 years and older living in low-and-middle-income countries for the years 2020 and 2040.

Cancer incidence estimates in adults aged 60 years and older living in low-and-middle-income countries for the years 2020 and 2040

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Abstract

Previous studies have shown a disproportionate rise in cancer incidence in low-and-middle-income countries (LMICs) due to rapid population ageing. This study aims to describe the cancer incidence in adults aged 60 years and older in LMICs to inform cancer control planning. Using the latest GLOBOCAN estimates for 2020, we describe the cancer incidence and the top five cancer sites among adults aged 60 years and older living in LMICs. We also project the incidence in 2040 by applying population projections, assuming no changes in incidence rates and risk profiles over time. In 2020, 6.3 million new cancer cases were diagnosed in older adults in LMICs, constituting over half of the global incidence burden (55%). In females aged 60 years and older living in LMICs, breast, lung, colon, stomach, and cervix uteri were the most frequent cancer types representing 51% of the total number of new cancer cases in older females. In males aged 60 years and older living in LMICs, lung, prostate, stomach, liver and colon were the most frequent cancer types representing 58% of the total number of new cancer cases in this subgroup. Variations were observed between income categories. The number of new cancer diagnoses in adults aged 60 years and older living in LMICs will almost double by 2040, reaching 11.5 million new cancer cases. The greatest increase is expected to happen in lower-income countries (+158% in lower-middle-income countries (excluding India) and +99% in low-income countries versus +38% in upper-middle-income countries). In conclusion, our findings call for an urgent adaptation of healthcare systems in LMICs by developing geriatric oncology and by including older adults in research, clinical guidelines, insurance schemes and cancer prevention policies.

Keywords: *neoplasms, incidence, older adults, geriatric oncology, epidemiology, low-and-middle-income countries, developing countries, aged*

Background

Due to global population ageing, the absolute number of older adults with cancer is increasing worldwide [1, 2]. This increase is disproportionately affecting less developed

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regions. A previous study showed an expected +144% increase in the number of older adults with cancer in less developed regions versus +54% in more developed countries between 2012 and 2035 [1].

Despite the increasing older populations in low-and-middle-income countries (LMICs) and the existence of global strategies on ageing and health such as that of the World Health Organisation (WHO) [3], older adults are generally under-represented in research, health and clinical programmes, and those with cancer are often not included when defining global healthcare priorities [4].

Because of the heterogeneity of the older population in terms of health status and fitness, the lack of geriatric expertise in the oncology workforce and the scarcity of evidence-based cancer management strategies [5], the rising number of older people with cancer brings along challenges and opportunities for healthcare systems worldwide. Furthermore, the capability of healthcare systems to respond depends greatly on the availability of resources, including not only infrastructure but also personnel.

LMICs are a heterogeneous group of countries between and within the World Bank income categories (low, lower-middle and upper-middle) in terms of demographic, healthcare system, infrastructures, medical and paramedical expertise, culture and traditions.

There is an urgent need to describe the cancer burden among the older population living in LMICs and to discuss their specific challenges to improve the allocation of resources to control the cancer burden in developing regions of the world.

Using 2020 GLOBOCAN estimates, we described cancer incidence estimates in adults aged 60 years and older living in LMICs. We also projected the number of new cancer cases expected to be diagnosed in adults aged 60 years and older living in LMICs in 2040.

Methods

Older adults were defined as adults aged 60 years and older, following the United Nations (UN) definition, which takes into account the characteristics of ageing in developing regions of the world [6].

LMICs were selected using the 2020 World Bank classification [7].

The estimated number of new cancer cases, as well as the population size for the year 2020 for the world and 185 countries, was extracted from the Global Cancer Observatory [8]. Data were available for 34 cancer types and all cancer sites combined, excluding non-melanoma skin cancer (ICD-10 C00-97, except C44), and for ten age groups (0-14, 15-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75 and over) by sex.

Numbers of new cases among adults aged 60 years and older and truncated age-standardised incidence rates for the 60-year-and-older age group (ASR per 100,000 inhabitants of the same age – world standard population of Segi, revised by Doll *et al* [9]) for all cancer sites combined and the five most common cancer sites were described for low-income, lower-middle and upper-middle World Bank income separately. Given their relative population sizes, estimates for China (upper-middle-income country) and India (lower-middle-income country) were presented separately.

We also computed the number of new cancer cases occurring in adults aged 60 years and older as a proportion of the total cancer diagnoses in both sexes and by sex, worldwide, and by the World Bank income group.

Finally, we predicted the future number of new cancer cases (all cancer sites combined) in adults aged 60 years and older worldwide and by World Bank income group for the year 2040 by applying sex- and age-specific incidence rates in 2020 to UN population projections using the medium-fertility variant for the year 2040 [10].

For our projections, we considered only the effect of ageing and population growth and assumed no change in the risk patterns of cancer incidence between 2020 and 2040.

Data analysis was conducted using R statistical software (version 4.2.2; R Development Core Team, 2022) [11].

Results

Overall cancer burden

In 2020, an estimated 6.3 million new cancer cases were diagnosed among adults aged 60 years and older living in LMICs (55.3% of cases in adults aged 60 and older worldwide), representing 55.6% of all new cancer cases (all ages combined) in LMICs (Table 1). This proportion increased as World Bank income increased, going from 39.2% in low-income countries to 59.3% in upper-middle-income countries (excluding China), with the proportion in lower-middle-income countries (excluding India) being in-between at 47.4%. The proportion of cancer cases diagnosed in adults aged 60 years and older in China (which alone accounted for 59% of all cases diagnosed in upper-middle-income countries) and India (43% of all cases diagnosed in lower-middle-income countries) were 60.0% and 47.8%, respectively.

At the country level, Bulgaria, an upper-middle-income country, had the highest proportion of total cancers diagnosed in adults aged 60 years and older (73%), and Malawi, a low-income country, had the lowest (23% – Supplemental Table 1 at <https://doi.org/10.6084/m9.figshare.22561162.v1>).

Truncated age-standardised incidence rates (ASR) in LMICs were 821 per 100,000 but varied greatly, going from 540 in lower-middle-income countries to 1,005 per 100,000 inhabitants aged 60 years and older in upper-middle-income countries (Figure 1). There were also great variations within World Bank income groups. In low-income countries, truncated ASRs varied between 312 per 100,000 in Niger to 834 per 100,000 in the Democratic People's Republic of Korea (Supplemental Table 1 at <https://doi.org/10.6084/m9.figshare.22561162.v1>). Truncated ASRs in lower-middle-income countries ranged from 374 in Djibouti to 1,243 in Mongolia, while in upper-middle-income countries, they ranged from 410 in Equatorial Guinea to 1,434 in Serbia.

Table 1. Number of new cancer cases, percentages of new cancer cases and adults aged 60 years and older, crude and truncated ASR among adults aged 60 years and older living in LMICs and worldwide by sex.

	Number of new cases among 60+*		Percentages of new cases among 60+ (%)		Percentages of population aged 60+ (%)		Crude incidence rate among adults aged 60+ (per 100,000)		Truncated age-standardised incidence rates among adults aged 60+ (per 100,000)	
	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
LMICs	2,748,000	3,509,000	49.3	61.7	12.3	10.4	689	1,015	668	1,007
Low-income countries	99,000	95,000	34.6	47.6	5.7	4.6	505	597	500	608
Lower-middle-income countries (excluding India)	378,000	427,000	42.4	52.9	8.5	7.1	562	763	553	763
India	292,000	336,000	43.3	52.6	10.7	9.6	411	491	407	491
Upper-middle-income countries (excluding China)	860,000	1,043,000	52.6	66.3	14.7	11.7	782	1,230	748	1,205
China	1,120,000	1,607,000	53.8	65.2	18.6	16.3	853	1,332	823	1,317
World	4,925,000	6,381,000	56.3	68.3	14.6	12.3	871	1,318	816	1,268

*Rounded to the nearest thousand

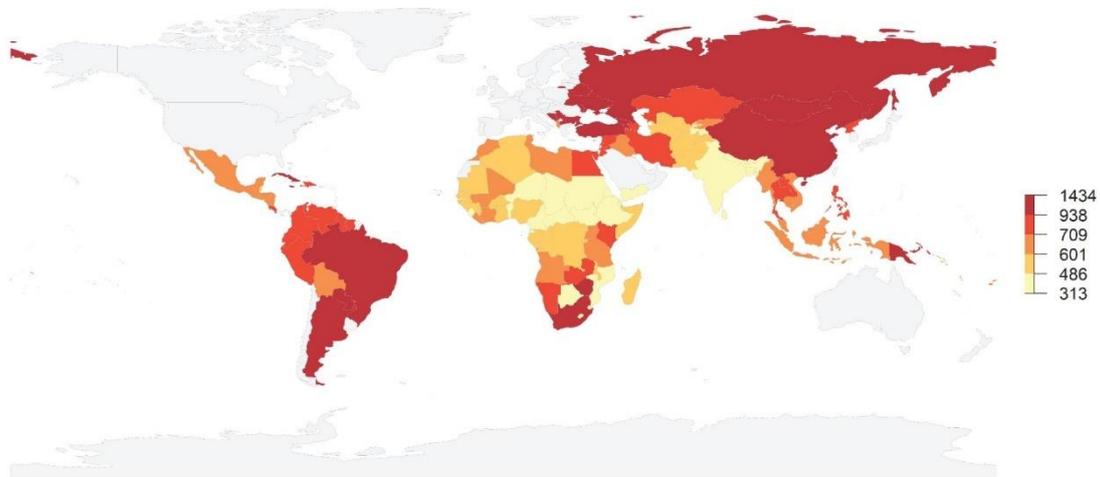


Figure 1. Map showing quantiles of estimated truncated age-standardised incidence rates for all types of cancers (excluding non-melanoma skin cancer – per 100,000 inhabitants) among adults aged 60 years and older living in LMICs in 2020. Estimates are shown for LMICs only. Grey colour indicates no value.

Cancer profile in older adults living in LMICs by sex

In females aged 60 years and older living in LMICs, breast, lung, colon, stomach, and cervix uteri were the most frequent cancer types and represented 50.8% of the total number of new cancer cases in this age group (Figure 2). The top five cancers were breast, cervix uteri, lung, stomach and liver cancers (55% of all cancers diagnosed in this age group) in low-income countries. In lower-middle-income countries (excluding India), the top three were the same as those in low-income countries, followed by liver and colon cancers (50%). The cancer profile was different in India with the five most common cancer types in females aged 60 years and older being breast, cervix uteri, ovarian, lip and oral cavity, and oesophageal cancers (56%). In upper-middle-income countries, breast, colon, lung, corpus uteri, and cervix uteri were the five most common cancer types (51%). In China, lung cancer was the most common cancer diagnosed in females aged 60 years and older, followed by breast, colon, stomach, and oesophageal cancers; with these cancers representing 57% of all cancers diagnosed in this age group. As a comparison, the most common cancer types worldwide in females aged 60 years and older were breast, lung, colon, stomach and corpus uteri (52%).

In males aged 60 years and older living in LMICs, lung, prostate, stomach, liver, and colon were the most frequent cancer types and represented 58% of the total number of new cancer cases in this age group (Figure 3). Like females, some differences were observed between World Bank income groups. In low- and lower-middle-income countries (excluding India), prostate, lung and stomach cancers were the three most common cancer types, followed by liver and oesophageal cancers in low-income countries and stomach and bladder in lower-middle-income countries. The top five cancers represented 58% and 54% of all cancer diagnosed in males aged 60 years and older, respectively. In India, cancers of the lip and oral cavity were the most frequently diagnosed in older males, followed by prostate, lung, oesophagus and stomach (45%). In upper-middle-income countries (excluding China), prostate, lung, colon, stomach and bladder cancers were the most frequent cancers, representing 61% of all cancers diagnosed in this population. Like females, lung cancer was the most common cancer type diagnosed in older males in China, followed by stomach, oesophagus, liver, and colon cancers. These top five sites accounted for 72% of all cancers diagnosed in older males in China. Worldwide, the top five cancers in males aged 60 years and older were prostate, lung, stomach, colon and liver, representing 57% of all cancer cases diagnosed in this age group.

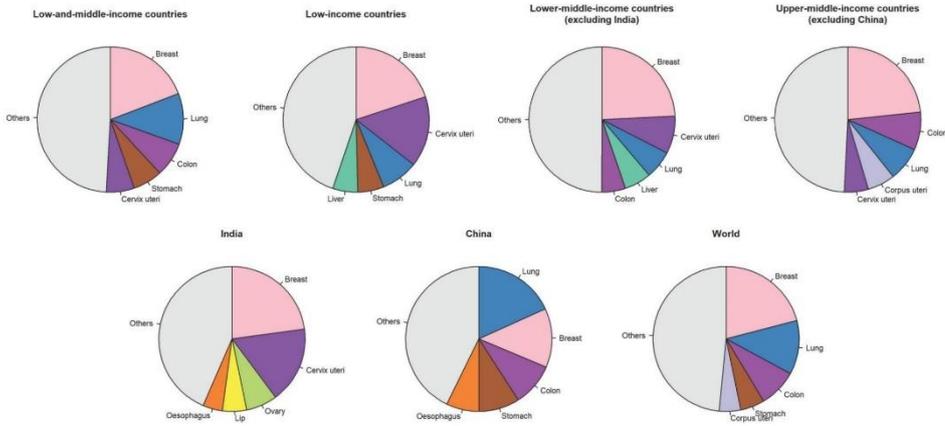


Figure 2. Pie charts representing the five most common cancer sites in females aged 60 years and older by World Bank income categories.

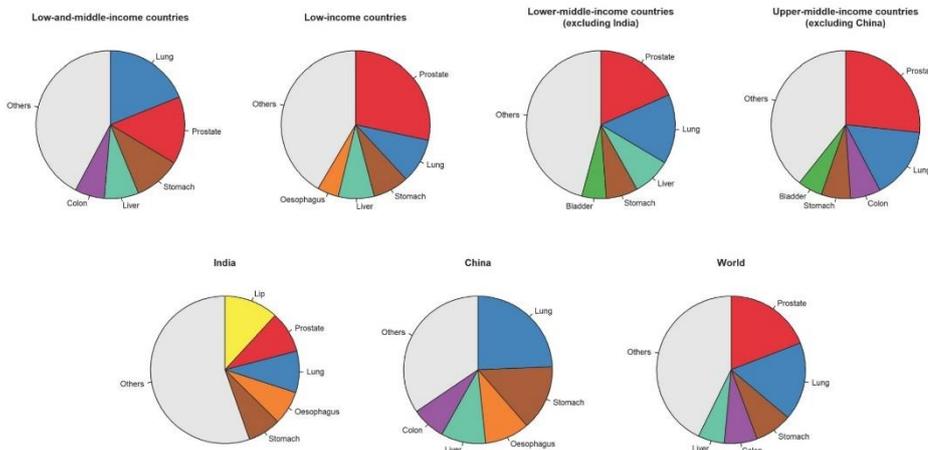


Figure 3. Pie charts representing the five most common cancer sites in males aged 60 years and older by World Bank income categories.

Projected number of new cancer cases in older adults living in LMICs by 2040 (Figure 4)

An estimated 11.5 million new cancer cases (66% of all cases, all ages combined) are expected to be diagnosed in adults aged 60 years and older living in LMICs by 2040, representing 57% of the worldwide expected number of cases in this age group.

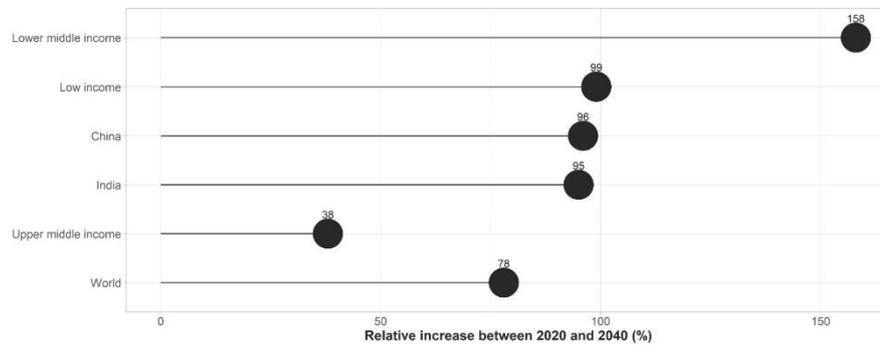


Figure 4. Estimated relative increase in the number of new cancer cases among adults aged 60 years and older living in LMICs between 2020 and 2040 (%).

Compared to the 2020 figure, this represents an expected increase of +84% in the number of new cancer cases aged 60 years and older living in LMICs (compared to an increase of +78% worldwide). The most significant increase is expected in lower-middle-income countries (excluding India) which can expect to see their number of cases in older adults increase by +158% (or an additional 1.3 million new cancer cases) in the next 20 years. Although this increase is expected to be more moderate in low-income countries, the number of new cancer cases is still expected to double by 2040 (+99%). In upper-middle-income countries (excluding China), the expected increase would be +38%. China and India will see the number of cancers diagnosed in adults aged 60 years and older double by 2040, with increases of +96% and +95%, respectively, or an additional 2.6 and 0.6 million new cancer cases aged over 60, respectively.

Discussion

Using the most up-to-date estimates from the global cancer observatory, we showed over 6 million new cancer cases (excluding non-melanoma skin cancer) were diagnosed in adults aged 60 years and older living in LMICs in 2020. This number is projected to reach 11.5 million in 2040 if the cancer risk pattern does not change over the period. The greatest increase is expected to occur in lower-middle-income countries (excluding India) which will see an increase of +158% in the number of cancer diagnoses among adults aged 60 years and older. Breast cancer in older females and lung and prostate cancers in older males were, by far, the most common cancer types diagnosed in 2020 regardless of the World Bank income category, except for China. The considerable increase in the number of cancer diagnoses among older adults in LMICs will pose a substantial strain on healthcare systems which will need to adapt quickly to offer optimum comprehensive care for ageing populations.

Infection-related cancers, mainly cervical cancers in older females, and gastric and liver cancers in both sexes were important contributors to the cancer burden in low-income and lower-middle-income countries. The importance of the contribution of colon cancer which is mainly caused by unhealthy dietary and physical activity habits is greater in upper-middle-income countries compared to other World Bank income categories. These differences in cancer patterns mean that preventive strategies need to be tailored to the local cancer profile. For example, strategies to reduce the likelihood of infection over the lifetime such as vaccination for hepatitis B, responsible for liver cancer, and Human Papilloma Virus, responsible for cervical cancers (as well as other malignancies), while benefitting future generations of older adults worldwide, would more significantly benefit those living in LMICs, where these cancer types are more common. In contrast, preventive interventions targeting smoking, obesity, physical inactivity and unhealthy diet throughout life, even at older ages [12–15], would have a greater impact in wealthier countries, although such interventions will be relevant for less-resourced countries as well.

As previously described for adults aged 65 years old [1], lung cancer is the most common cancer site diagnosed in both females and males aged 60 years and older in China. The high prevalence of smoking is likely to explain this finding in Chinese males but not in Chinese females, who have low smoking rates [16]. Lung cancer in Chinese females may, however, be caused by exposure to second-hand smoke, household air pollution originating from heating stoves using biomass, coal and other solid fuels, or outdoor air pollution particulate matter [17]. The State Council of China enacted the 'Air Pollution Prevention and Control Action Plan' in 2013 to lower the particulate matter level and a recent study showed an encouraging reduction in chronic conditions of the respiratory and circulatory systems [18]. This may also reduce the risk of lung cancer in future cohorts of older adults. However, this could be counterbalanced by an increasing trend in smoking in younger generations of Chinese males [16].

Many LMICs face a lack of infrastructure, access to anti-cancer treatment, oncologists and radiotherapists to offer optimal cancer management, regardless of the age of the patient. In addition, cancer management in older adults requires geriatric expertise, which is crucially lacking across many LMICs [19]. While some initiatives, such as those from the International Society for Geriatric Oncology (SIOG) offer geriatric oncology training in some LMICs [20], there is a huge need to be innovative in delivering care to older adults with cancer in low-resource settings. Such interventions could include the involvement of nurses or community health workers who can be trained in performing a geriatric assessment and implementing evidence-based interventions. Many models of care already exist for providing care that includes geriatric principles for older adults with cancer, and randomised clinical trials have shown that such interventions may lead to improved outcomes [21]. However, those studies have been performed in high-income countries, and research on how best to implement geriatric oncology in LMIC settings, including the use of innovative technologies such as telemedicine or mobile health, is urgently needed. Such research would certainly require adequate funding and global collaboration, and as such, this represents one of the highest priorities for the global development of geriatric oncology according to SIOG [22].

Offering palliative and supportive care for patients and their families represents a human right and is becoming increasingly important in high-income countries. Still, it remains a low priority and an under-researched area in LMICs, especially in older adults [23]. This represents a huge gap in cancer care since it is foreseeable that a significant proportion of older patients diagnosed with cancer in LMICs will present with advanced disease, where preserving quality of life, alleviating pain, and controlling symptoms is the most important and relevant goal. The Multinational Association of Supportive Care in Cancer defines supportive care as '*the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms and side effects across the continuum of the cancer journey from diagnosis through treatment to post-treatment care*' [24]. Resource-stratified guidelines as those proposed by the Breast Health Global Initiative, but tailored to the unique needs of older adults and their caregivers would help offer optimal supportive care for the increasing ageing population living in LMICs [23].

Based on the Global Atlas of Palliative Care, only half of the countries in the world, regardless of the World Bank income category, have an operational non-communicable disease plan including palliative care [25]. While 91% of high-income countries have dedicated funding for palliative care within their healthcare systems, this only happens in 48% of low-income countries [25]. When it comes to effective access to palliative care, 27% of patients living in upper-middle-income countries had access to palliative care, but only 3% and 1%, respectively in lower-middle-income and low-income countries (against 69% in high-income countries) [25].

The forecasted increase in cancer incidence among older adults in LMICs will also pose a considerable financial burden on households. Older adults in many LMICs support their families and are still active, mainly doing informal or unpaid jobs [26]. In addition, the costs of cancer diagnosis, care, and curative or palliative treatment are high and universal health coverage is not a reality for many LMICs. Between 18% and 93% of patients with cancer in LMICs face objective financial toxicity [27], and older patients with cancer have a higher likelihood of catastrophic health expenditure [28]. Implementing a health financing system to reduce (or avoid) out-of-pocket payments should be a priority in every country.

Our study has limitations. The definition of older adults differs between disciplines (e.g., medicine versus economics) and settings due to different life experiences and risk profiles. For instance, although the age of 50–55 was suggested to 'define' an older adult living in Africa, where life expectancy is lower [29], this would not be appropriate for super-aged societies such as Japan. However, for the purpose of description, we chose to use the UN definition of 60 years and older. Although we acknowledge this age cut-off may not be relevant in some settings, we believe it is the one that most correctly captures the current panorama of ageing in developing regions.

As described in Ferlay *et al* [30], many LMICs have no cancer registry and Globocan estimates are based on incidence data from neighbouring countries or from cause-specific mortality data. Mortality data relies on the accuracy of the cause of death reported on the death certificate when they exist. Identifying the cause of death may be challenging in older adults because of other fatal conditions, for instance. There is a risk of under-ascertainment of cancer cases in older adults which would mean that rates and the number of cases would be underestimated.

Finally, our projections of the number of cancer cases in older adults in LMICs in 2040 did not consider trends in cancer incidence and changes in risk factors. However, the possible decrease in infection-related cancers in LMICs in the next decades will likely be compensated by an increase in the incidence of lifestyle-related cancers, especially in countries in epidemiological transition [31, 32].

Conclusion

Most older adults with cancer already live in LMICs, and their number is still rising, especially in less-resourced countries, and this will greatly increase during the next 20 years. To close the cancer care gap and improve outcomes, it is urgent to include older adults with cancer in national, regional, and global cancer control policies. This should ideally lead to the development of age-friendly healthcare systems, with geriatric expertise embedded into each and every aspect of care as recommended by the WHO. To achieve this, researchers, clinicians and policymakers should take into account SIOG recommendations and foster the development of geriatric oncology resources that are tailored to each country's needs, priorities, and resources [22].

List of abbreviations

ASR: age-standardised rates; LMIC: Low-and-middle-income countries; SIOG: International Society for Geriatric Oncology; UN: United Nations; WHO: World Health Organisation.

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Conflicts of interest

The author(s) declare that they have no conflict of interest.

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Author contribution

SP: Conceptualisation; formal analysis; writing – Original draft; writing – review and editing; visualisation.

FG, VR, ES: Writing – Review and editing.

Data availability

Incidence data and 2020 population size are openly accessible at <https://gco.iarc.fr/> and the population size projections for the year 2040 are available at <https://population.un.org/wpp/>.

Ethical considerations

All data used in this work are publicly available; ethics approval was not required.

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Annexe 3: Protocole d'étude sur les facteurs associés au diagnostic tardif des cancers du sein au Bénin

FACTEURS ASSOCIES AU DIAGNOSTIC TARDIF DES CANCERS DU SEIN AU BENIN

Version de Janvier 2024

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Introduction

Dans le monde, le cancer du sein est le premier cancer de la femme aussi bien en terme d'incidence que de mortalité et constitue un problème de santé publique (Forouzanfar et al., 2011). Bien que l'incidence en ASS soit parmi les plus faibles au Monde, la mortalité y est parmi les plus élevées témoignant d'une survie médiocre. En 2020, l'ASS a enregistré 1.109.209 cas (dont 49339 cas en Afrique de l'ouest) pour 25.626 décès (Adeloye et al., 2018). Ces taux d'incidence et de mortalité devraient augmenter significativement au cours des prochaines années pour atteindre 3.000.000 de nouveaux cas et 1.000.000 de décès chaque année du seul fait de la croissance démographique et du vieillissement (Arnold et al., 2022).

Au Bénin, le cancer du sein vient au premier rang des cancers de la femme, aussi bien en terme d'incidence que de mortalité, avant celui du col utérin (Egue et al., 2019). Le pronostic du cancer du sein est influencé par plusieurs facteurs dont le stade au diagnostic.

Malgré les progrès importants réalisés à l'échelle mondiale ces dernière années dans le domaine du dépistage, 70 % des cas diagnostiqués en Afrique au Sud du Sahara le sont à des stades tardifs posant un réel problème de prise en charge thérapeutique (Pace et al., 2015). Des données plus récentes au Bénin montrent que plus de 65% des patientes avaient des tumeurs aux stades III ou IV (Todjinou, 2018).

Objectifs

Objectif général

Étudier les facteurs associés au diagnostic tardif des cancers du sein.

Objectifs spécifiques

- Estimer la fréquence du diagnostic tardif des cancers du sein
- Décrire les caractéristiques sociodémographiques des femmes atteintes de cancers du sein au stade tardif
- Décrire le parcours de soins des patientes atteintes de cancers du sein

Problématique

Enoncé du problème

Le cancer du sein est le premier cancer de la femme en Afrique au Sud du Sahara et la première cause de mortalité par cancer chez la femme (Desreux, 2018). En effet, bien que l'incidence de la maladie en Afrique au Sud du Sahara semble plus faible, les taux de mortalité sont



disproportionnellement élevés par rapport aux pays à revenu élevé (Anyigba et al., 2021). De même le taux de mortalité par cancer du sein en Afrique au Sud du Sahara est élevé car plus de la moitié sont diagnostiqués tardivement à des stades localement avancés ou métastatiques (Espina et al., 2017; Pace et al., 2015; Tesfaw et al., 2021). Ceci est dû aux retards de diagnostic et de traitement (Joko-Fru, Miranda-Filho, et al., 2020). Selon une étude réalisée en Côte d'Ivoire et en République du Congo, la proportion de cancer du sein diagnostiqué aux stades tardifs (III et IV) était respectivement de 74% et 81 % (Islami et al., 2015). Par ailleurs, il faut noter qu'il y a un délai considérable entre les premiers symptômes et la consultation chez un professionnel de la santé (Joko-Fru, Miranda-Filho, et al., 2020). Une revue systématique a documenté un retard de consultation entre 3 et plus de 6 mois et un retard supplémentaire de 3 à 6 mois entre la première consultation chez un professionnel de la santé et la confirmation du diagnostic de cancer du sein en Afrique au Sud du Sahara (Jedy-Agba et al., 2016). De plus, d'autres études réalisées en Afrique ont noté un délai médian élevé entre la reconnaissance des premiers symptômes et le diagnostic du cancer du sein. Ce délai a été estimé à 7,9 mois à Accra au Ghana (Clegg-Lampsey et al., 2009), à plus de 10 mois à Abidjan en Côte d'Ivoire (Toure et al., 2013) et à 15 mois dans les zones rurales du Rwanda (Pace et al., 2015). En comparaison, en Europe notamment au Danemark, le délai médian entre la première consultation dans un établissement de santé et le diagnostic était en moyenne de 25 jours (IIQ : 14-44 jours) (Joko-Fru, Miranda-Filho, et al., 2020). Aussi, environ 30 % de tous les cas de cancer du sein en Angleterre, en Écosse et au Pays de Galles ont-ils été identifiés

à la phase asymptomatique par dépistage . Le retard de consultation et le diagnostic à un stade tardif sont des défis courants dans les pays à revenu faible et intermédiaire comme le Bénin. Le pronostic reste généralement plus favorable pour les femmes atteintes d'un cancer à un stade plus précoce que celles dont le cancer est à un stade plus avancé (Caplan, 2014). Également les moyens thérapeutiques ainsi que le coût du traitement dépendent du stade du cancer du sein. De nos jours, la plupart des cytotoxiques recommandés pour traiter le cancer du sein à un stade avancé sont efficaces en termes de réponse objective et de survie globale mais leur disponibilité et leur accessibilité posent problèmes dans les pays en voie de développement à cause de leur coût très élevés (Diallo et al., 2022). Les cancers du sein de stade IV sont incurables et les objectifs du traitement comprennent essentiellement la stabilisation de la maladie, l'allongement de la survie sans progression et l'amélioration de la qualité de vie de la patiente (Erfani et al., 2021). La mortalité étant moindre chez les patientes diagnostiquées précocement, il s'avère donc nécessaire de baser les stratégies de prise en charge sur le dépistage et le diagnostic précoce (Caplan, 2014). De telles stratégies ne peuvent se concevoir sans une identification des facteurs associés au diagnostic tardif.

Certaines études ont identifié des facteurs associés au diagnostic tardif des cancers du sein. En 2013 en Côte d'Ivoire, le manque de moyens financiers, les habitudes socio-culturelles, les erreurs diagnostiques, le caractère inflammatoire des cancers étaient les facteurs associés au diagnostic tardif du cancer du sein (Toure et al., 2013). En 2020 au Togo, les facteurs identifiés étaient la peur du diagnostic, l'absence d'auto-examen des seins, le recours au traitement traditionnel et l'automédication en première intention (Darré et al., 2023). La présente étude est menée afin de mesurer, au Bénin, la fréquence du diagnostic tardif chez les patientes atteintes de cancers du sein et d'identifier les facteurs associés. Les résultats de cette étude permettront de mettre en place des actions de prévention efficaces pour réduire la morbidité et la mortalité liées aux cancers du sein au Bénin.

Cadre d'étude

Il s'agira des centres de références hospitaliers du Bénin notamment le CNHU-HKM et le CHUMEL de Cotonou.

Méthodologie de recherche

Type et période d'étude

Il s'agira d'une étude transversale descriptive et analytique avec collecte des données sur une période de 1 an.

Population d'étude

La population d'étude sera constituée de toutes les femmes atteintes de cancer du sein et ayant consulté dans l'un des centres de référence pendant la période d'étude.

Critères d'inclusion

Les critères d'inclusion seront les suivants :

- Patientes atteintes de cancer du sein histologiquement confirmé ;
- Ayant consulté dans l'un des services concernés pendant la période d'étude ;
- Ayant donné leur consentement éclairé.

Critères de non inclusion

- Patientes ayant un état général altéré avec un Indice de Performance Status (IPS OMS= 4);
- Patientes avec troubles psychiatriques sévères.

Echantillonnage

• Technique d'échantillonnage

Nous procéderons à un recrutement exhaustif de toutes les patientes répondant à nos critères d'étude.

Définition des variables

● Variable dépendante

La variable d'intérêt sera le Stade au diagnostic. Elle présentera deux modalités : précoce et tardif. Le diagnostic sera dit tardif lorsqu'il est posé à un stade évolué ou d'emblée métastatique soit stade III et IV de la classification de l'AJCC. Le diagnostic sera dit précoce lorsqu'il est posé aux stades I ou II de l'AJCC.

● Variables indépendantes

Les variables indépendantes seront regroupées en variables sociodémographiques, cliniques et paracliniques ; en variables liées à la connaissance et la sensibilisation sur le cancer du sein; en variables liées à l'accès aux services de dépistage et en variables liées aux caractéristiques socio-culturelles. Elles se présenteront comme suit :

- Variables sociodémographiques : âge, revenu, assurance maladie, situation matrimoniale, niveau d'instruction, zone de résidence, département de résidence.
- Variables cliniques : motif de consultation, symptôme inaugural, délai de consultation médicale, délai diagnostique, premier recours, premier agent de santé consulté, nombre de formations sanitaires parcourues avant le diagnostic, existence d'une erreur diagnostique, stade du cancer.
- Variables paracliniques : type histologique du cancer, grade histopronostique du cancer, délai du diagnostic histologique.
- Variables relatives à la connaissance et la sensibilisation sur le cancer du sein : information sur le cancer du sein, sources d'information sur le cancer du sein.
- Variables liées à l'accès aux services de dépistage : dépistage antérieur du cancer du sein, pratique de l'autopalpation.
- Variables socio-culturelles liées au cancer du sein : Représentation socio-culturelle de la maladie, ressenti avant le diagnostic du cancer de sein.

- **Opérationnalisation des variables**

Tableau I : Aspect opérationnel des variables sociodémographiques des patientes

Variables	Définition	Type de variable	Modalités
Age	Nombre d'années de la naissance au moment de la collecte	Quantitative discrete	###
Revenu	Somme d'argent gagnée par mois	Qualitative nominale	1. Sans revenu 2. \leq SMIG 2-3*SMIG 3. $>$ SMIG
Assurance maladie	Protection financière contre les coûts liés aux soins de santé	Qualitative binaire	1. Oui 2. Non
Situation matrimoniale	Statut marital	Qualitative binaire	1. Mariée 2. Veuve 3. Divorcée 4. Célibataire 5. Concubinage
Niveau d'instruction	Niveau d'étude actuel ou atteint	Qualitative nominale	1. Non scolarisée 2. Primaire 3. Secondaire /technique 4. Supérieur
Zone de résidence	Lieu d'habitation de la patiente	Qualitative binaire	1. Ville 2. Capitale 3. Village



Tableau II : Aspect opérationnel des variables cliniques des patientes

Variables	Définition	Type de variable	Modalité
Motif de consultation	Symptôme ayant motivé la consultation	Qualitative nominale	1. Nodule 2. Inflammation 3. Aspect peau d'orange 4. Ulcération 5.Écoulement mamelonnaire 6. Métastases révélatrices 7. Autres (préciser)
Symptôme inaugural	Premier symptôme perçu au début de la maladie	Qualitative nominale	1. Nodule 2. Inflammation 3. Aspect peau d'orange 4. Ulcération 5.Écoulement mamelonnaire 6. Métastase révélatrice 7. Autres (préciser)
Délai de consultation médicale	Période entre la constatation du premier symptôme et la première consultation médicale (en jours)	Quantitative continue	###
Délai diagnostique	Période entre la constatation du premier symptôme et la confirmation histologique de cancer du sein	Quantitative continue	###
Premier recours	Premier lieu ou centre consultée	Qualitative nominale	1. Tradithérapeute 2. Pratiques religieuses 3. Médecine alternative 4. Médecine conventionnelle *1 ou 2 ou 3 = médecine non conventionnelle
Premier agent de santé consulté	Qualité du premier personnel de santé consulté		1. Médecin spécialiste (à préciser) 2. Médecin généraliste 3. Sage-femme 4. Infirmier



Variables	Définition	Type de variable	Modalités
Le nombre de formations sanitaires parcourues avant le diagnostic		Quantitative discrète	###
Erreur diagnostique antérieure	Autre diagnostic antérieurement posé en dehors du cancer	Qualitative binaire	1. Oui 2. Non
Stade du cancer	Stade du cancer du sein au moment du diagnostic	Qualitative continue	1. Stade 1 2. Stade 2 3. Stade 3 4. Stade 4

Tableau III : Aspect opérationnel des variables paracliniques des patientes

Variables	Définition	Type de variable	Modalités
Type histologique du cancer		Qualitative nominale	1. Carcinome non spécifique in situ 2. Carcinome non spécifique infiltrant 3. Carcinome lobulaire in situ 4. Carcinome lobulaire infiltrant
Grade histopronostique	Evaluation pathologique selon SBR qui classe les cellules cancéreuses en fonction de leur degré de différenciation et d'agressivité.	Qualitative nominale	1. Grade 1 2. Grade 2 3. Grade 3
Délai du système de santé	Période entre la première consultation médicale et la confirmation histologique de diagnostic de cancer du sein.	Quantitative continue	###

Tableau IV : Aspect opérationnel des variables concernant la connaissance et la sensibilisation sur le cancer du sein

Variables	Définition	Type de variable	Modalités
Information sur le cancer du sein	Avoir entendu parler du cancer de sein	Qualitative binaire	1. Oui 2. Non
Sources d'information sur le cancer du sein		Qualitative nominale	1. Médias 2. Amis ou familles 3. Campagne de sensibilisation 4. Professionnels de santé 5. Autres

Tableau V : Aspect opérationnel des variables liées à l'accès aux services de dépistage du cancer du sein

Variables	Définition	Type de variable	Modalité
Dépistage antérieur du cancer du sein	Avoir bénéficié d'un dépistage du cancer du sein avant le diagnostic	Qualitative nominale	1. Oui 2. Non
Pratique de l'auto-palpation	Palpe les seins chaque mois	Qualitative binaire	1. Oui 2. Non

Tableau VI : Aspects opérationnels des variables socio-culturelles et psychologiques liées au cancer du sein

Variables	Définition	Type de variable	Modalité
Représentation du cancer du sein	C'est la conception personnelle en ce qui concerne le cancer du sein	Qualitative nominale	1. Sorcellerie 2. Puniton divine 3. Affection médicale banale 4. Affection médicale grave
Ressenti avant le diagnostic du cancer du sein		Qualitative nominale	1. Confiante 2. Peur du diagnostic 3. Peur du traitement

Collecte des données

- **Technique et outil de collecte des données**

La collecte des données se fera via un entretien individuel en mode face à face complété par une revue des observations médicales.

L'outil de collecte sera une fiche d'enquête préalablement établie et digitalisée avec koboCollect.

- **Déroulement de la collecte**

La collecte sera effectuée par un médecin. Nous ferons un pré-test du questionnaire sur huit (08) patientes puis nous l'ajusterons. Dans un premier temps le consentement éclairé des patientes répondant à nos critères d'inclusion sera recueilli puis nous procéderons à l'administration du questionnaire. Les informations complémentaires (stade au diagnostic, type histologique et le grade histo-pronostique du cancer) seront renseignées à partir de l'observation médicale des patientes. La collecte des données sera faite sous la supervision d'un médecin spécialiste en oncologie.

Traitement et analyse statistiques

Les données seront exportées de koboCollect vers Excel 2016, puis nettoyées et les variables codifiées. L'analyse des données sera effectuée à l'aide du logiciel R. Les variables quantitatives seront présentées sous forme de moyenne accompagnée de l'écart-type ou de la médiane avec intervalle interquartile, selon leur distribution (normale ou non). Les variables qualitatives seront exprimées en nombre d'occurrences et en pourcentage.

Pour évaluer l'association entre les variables indépendantes et la variable dépendante (le stade au diagnostic), des analyses bivariées seront menées. Les comparaisons de proportions seront effectuées à l'aide du test du chi carré, du test exact de Fisher ou du test corrigé de Yates en fonction des conditions spécifiques appropriées à chaque test, tandis que les différences entre les moyennes seront évaluées avec le test t de Student. Les comparaisons de médianes seront réalisées à l'aide du test de Wilcoxon. Dans le cadre de l'analyse bivariée des variables indépendantes, une régression logistique simple sera utilisée pour calculer les rapports de cotes (Odds Ratio). Le seuil de significativité statistique sera fixé à 5%.

Pour l'analyse multivariée, un modèle initial de régression logistique binaire sera construit, intégrant les variables indépendantes avec une valeur p inférieure à 0,20 en analyse bivariée. Ensuite, une régression pas à pas descendante (backward stepwise regression) sera réalisée pour simplifier ce modèle initial en retirant progressivement les prédicteurs non statistiquement significatifs. L'association entre les facteurs identifiés et la variable d'intérêt sera évaluée à l'aide de l'odds ratio (OR) et de son intervalle de confiance à 95% (IC95%). Un seuil de significativité de 5%

(p-value < 0,05) sera retenu. La validité du modèle final sera évaluée à l'aide du test de Hosmer-Lemeshow.

Considérations éthiques

Le protocole d'étude sera soumis au Comité d'Éthique de Recherche en Sciences de Santé (CERSS) pour avis et approbation.

L'accord des autorités administratives compétentes des différents hôpitaux sera obtenu. La confidentialité sera rigoureusement respectée lors de l'enquête. L'accès à la base de données numérique sera strictement limité et réservé à l'équipe de recherche. Le libre consentement des enquêtées sera également respecté en ce qui concerne l'administration du questionnaire aux patientes et la prise d'image chez certaines d'entre elles.

Budget prévisionnel

Poste budgétaire	Description exacte	Montants en Euros
Frais d'investissement	Frais d'équipement pour l'analyse des données et la rédaction d'articles scientifiques (ordinateurs, achat de logiciels, accès internet aux bases de données)	1237
Frais comité d'éthique	---	76
Frais administratif	Attachés de la recherche	122
Frais de personnel	Frais divers (collaborateurs, déplacements, communication)	305
Marge pour prévision budgétaire insuffisante	---	153
Total	-	1893



Annexe 4 : Avis éthique ; Génétique des cancers du sein au Bénin : recherche de mutations délétères constitutionnelles et acquises



IRSP
Institut Régional de Santé Publique



UNIVERSITE D'ABOMEY-CALAVI
COMITE D'ETHIQUE ET DE RECHERCHE DES SCIENCES DE LA
SANTÉ (CER-SS)

N° 007-2021/UAC/CERSS/P/SG/R/SA

Cotonou le 17 décembre 2021

AVIS ETHIQUE

Le Comité d'Ethique et de Recherche des Sciences de la Santé (CERSS), en sa session du 17 décembre 2021 a étudié le dossier du projet de recherche « **Génétique des cancers du sein au Bénin : recherche de mutations délétères constitutionnelles et acquises** » soumis par **FASSINOU Rose-Mariane**.

Ledit projet respecte les principes éthiques fondamentaux mais la composition du dossier de soumission n'est pas conforme aux critères d'évaluation du CERSS.

En conséquence, le CERSS émet un **avis favorable sous réserve** de la prise en compte des observations suivantes (à mettre à disposition du CERSS) :

- fournir l'engagement des auteurs à respecter l'avis éthique
- compléter la note d'information (Mieux renseigner la note d'information sur les risques (une biopsie est invasive) encourus et dire comment ces risques seront pris en charge)



Le Président

Prof Francis DOSSOU

Annexe 5: Avis éthique ; Etude de survie dans les cancers du sein chez la femme au CNHU et au
CHU-MEL de Cotonou



UNIVERSITÉ D'ABOMEY-CALAVI
COMITÉ D'ÉTHIQUE POUR LA RECHERCHE EN SCIENCES DE
LA SANTÉ (CERSS)

N° 017-2021/UAC/CERSS/P/SG/R/SA

Cotonou le 23 décembre 2021

AVIS ETHIQUE

Le Comité d'Éthique et de Recherche des Sciences de la Santé (CERSS), en sa session du 23 décembre 2021 a étudié le dossier du projet de recherche « **Etude de survie dans les cancers du sein chez la femme au CNHU et au CHU-MEL de Cotonou** » soumis par **GNANGNON Freddy Houéhanou Rodrigue**.

Ledit projet respecte les principes éthiques fondamentaux mais la composition du dossier de soumission n'est pas conforme aux critères d'évaluation du CERSS.

En conséquence, le CERSS émet un **avis favorable sous réserve** de la prise en compte des observations suivantes (à mettre à disposition du CERSS) :

- Fournir deux évaluations scientifiques assorties des CV des évaluateurs
- Fournir le formulaire de soumission du dossier pour avis éthique dûment rempli.

Le Président



Prof Francis DOSSOU

Annexe 6 : Avis éthique ; Epidémiologie descriptive des cancers du sein à Cotonou



IRSP
Institut Régional de Santé Publique



UNIVERSITE D'ABOMEY-CALAVI
COMITE D'ETHIQUE ET DE RECHERCHE DES SCIENCES DE LA
SANTÉ (CER-SS)

N° 005-2021/UAC/CERSS/P/SG/R/SA

Cotonou le 17 décembre 2021

AVIS ETHIQUE

Le Comité d'Éthique et de Recherche des Sciences de la Santé (CERSS), en sa session du 17 décembre 2021 a étudié le dossier du projet de recherche « **Epidémiologie descriptive des cancers du sein à Cotonou** » soumis par **GNANGNON Freddy Houéhanou Rodrigue**.

Ledit projet respecte les principes éthiques fondamentaux mais la composition du dossier de soumission n'est pas conforme aux critères d'évaluation du CERSS.

En conséquence, le CERSS émet un **avis favorable sous réserve** de la prise en compte des observations suivantes (à mettre à disposition du CERSS) :

- deux avis scientifiques qui respectent le canevas du CERSS
- CV des évaluateurs scientifiques
- engagement à respecter l'avis du comité d'éthique



Le Président

Prof Francis DOSSOU

Scanné avec CamScanner

Annexe 7 : Protocole d'étude sur la recherche de mutation génétique délétère chez la femme atteinte d'un cancer de sein au Bénin

**RECHERCHE DE MUTATION GENETIQUE DELETERE CHEZ LA FEMME
ATTEINTE D'UN CANCER DE SEIN AU BENIN**

Investigateur Principal

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INTRODUCTION

Le cancer du sein est le premier cancer en termes d'incidence, de prévalence et de mortalité tout sexe confondu en Afrique subsaharienne. Véritable problème de santé publique, le cancer du sein est le cancer le plus diagnostiqué au monde depuis trois ans. Avec plus de 129 400 nouveaux cas en 2020, il est le premier cancer de la femme dans 27 des 48 pays d'Afrique au Sud du Sahara et la première cause de mortalité par cancer chez la femme dans 19 de ces pays (Bray et al., 2022). Avec une population estimée à 1,18 milliards d'habitants pour 48 pays, l'Afrique au Sud du Sahara (ASS) représente 14 % de la population mondiale (Gnangnon, 2023). Cette population pourrait doubler d'ici à 2050 et atteindre 22 % de la population mondiale (Gnangnon, 2023).

Aussi remarquons nous que malgré que les taux d'incidence en Afrique au Sud du Sahara soient parmi les plus bas au monde, les taux de mortalités y sont les plus élevés. Plusieurs facteurs pourraient expliquer ce constat. Une revue systématique et méta-analyse identifie le stade tardif, un jeune âge et le cancer du sein triple négatif comme facteurs péjoratifs le plus souvent retrouvés (Gnangnon et al., 2023).

Au Bénin, une étude réalisée sur l'âge du diagnostic des cancers du sein montre que la majorité des patientes atteintes avaient moins de 50ans au moment du diagnostic histologique, une moyenne de 47,45ans et une tranche de 40ans à 50ans plus représentative (Gnangnon et al., 2020).

De même, l'étude du profil épidémiologique, moléculaire et pronostic du cancer du sein au sud du Bénin révèle que les patientes étaient relativement jeunes avec un âge moyen de 48,8ans, avec un antécédent familial de cancer de sein dans 11,8% des cas (Gnangnon et al., 2020). La majorité des cancers sont classés au stade III (42,2%) et IV (22,8%) (Gnangnon et al., 2020). De manière surprenante, le type de cancer le plus fréquent est le type triple négatif (32% versus 10% en Europe), cancer du sein très agressif n'exprimant pas les récepteurs hormonaux (ER-, PR-, et HER2-) (Gnangnon et al., 2020). Ces constats font suspecter des causes génétiques impliquées dans la genèse du cancer de sein chez la femme béninoise.

Objectifs

Général : Etudier les mutations génétiques délétères chez les femmes atteintes d'un cancer du sein au Bénin.

Spécifiques :

1-Identifier les mutations constitutionnelles ou acquises impliquées dans la prédisposition au cancer du sein au Bénin

1-Cadre Et Méthode D'étude

1-1-Cadre d'étude

- Le Centre National Hospitalier Universitaire Hubert KOUTOUKOU MAGA (CNHU-HKM) de Cotonou
- Le centre hospitalier universitaire de la mère et de l'enfant (CHU-MEL)
- Le laboratoire d'Histologie, de Biologie de la Reproduction, Cytogénétique et Génétique Médicale (LHBRCGM) à Cotonou,
- Le laboratoire d'Épidémiologie des Maladies Chroniques en zone Tropicale (EpiMaCT) à Limoges en France.

1-2-Méthode d'étude

Type d'étude : il s'agira d'une étude transversale descriptive

Période d'étude : les patientes seront recensées de mai à octobre 2024

Population d'étude :

Il s'agira de collecter les prélèvements tissulaires (biopsiques ou pièces opératoires tumorales) de tumeur de patientes atteintes d'un cancer du sein histologiquement confirmé.

Sélection et exclusion des sujets

Critères d'inclusion : seront incluses, les patientes prises en charge au CNHU/HKM ou au CHU-MEL pour une tumeur de sein confirmée par l'examen anatomopathologique.

Critères de non inclusion : les patientes n'ayant pas donné leur consentement éclairé.

Nombre de sujets nécessaires

La taille sera déterminée par commodité. Il est prévu d'inclure au moins 50 patientes atteintes du cancer du sein dans l'étude. Il s'agira d'un échantillonnage non probabiliste de convenance.

Recueils des données

Les données seront recueillies grâce à un entretien face à face avec les patientes, les dossiers des patientes, des comptes-rendus d'examen anatomo-pathologique et d'imagerie médicale. Nous utiliserons comme outils de collecte des fiches d'enquêtes.

Description des variables

Les variables socio-démographiques :

- L'âge : exprimé en années révolues
- La profession
- Le niveau d'instruction,
- Ethnie : sera reportée et ensuite une catégorisation en principaux groupes ethnolinguistiques

Les caractéristiques cliniques :

Le motif de consultation,
Les caractéristiques de la tumeur,
Les antécédents personnels,
Les antécédents familiaux

La caractéristique paraclinique étudiée sera le type histologique.

Conservation et gestion des données

Les formulaires remplis seront stockés dans une armoire verrouillée au niveau du Laboratoire d'Épidémiologie des Maladies Chroniques et Neurologiques (LEMACEN) à la Faculté des Sciences de la Santé. Leur accès sera limité aux seules personnes autorisées. L'accès à la base de données numérique sera strictement limité et réservé à l'équipe de recherche. Elle sera conservée dans un ordinateur, et protégée par un nom d'utilisateur et un mot de passe. Les fichiers seront anonymes et codés avant tout transfert par support électronique ou e-mail.

Conservation des fragments tissulaires

Les fragments tissulaires issus d'une micro biopsie ou d'un prélèvement tissulaire seront conservés dans du sérum physiologique stérile et acheminé immédiatement au laboratoire LHBRCGM. L'échantillon sera congelé à -20°C.

Extraction de l'ADN à partir de biopsie

L'extraction se fera en suivant le manuel du kit DNeasy Blood & Tissue Kit. Après avoir décongelé un fragment de biopsie, 25 mg de tissu seront coupés à l'aide d'un scalpel et déposés dans un tube Eppendorf de 1,5ml. 180µl de tampon ATL et 20µl de protéinase K seront déposés dans le tube Eppendorf de 1,5ml contenant le tissu. Le mélange obtenu sera ensuite vortexé et incubé à 56°C pendant 3 heures jusqu'à dissolution complète du tissu.

Après cette étape de digestion complète, 200µl de tampon AL sera complété au produit puis porté sur vortex pendant 15s. Le mélange obtenu sera incubé à 70°C pendant 10min. Le nouveau mélange obtenu sera centrifugé brièvement puis 200µl d'éthanol absolue sera ajouté et vortexé pendant 15 secondes. Le mélange obtenu sera déposé sur une mini colonne QIAamp et centrifugé à 8000 tours / minute pendant 1min 30 secondes. À la fin de la centrifugation le tube collecteur sera vidé. Sur la mini colonne QIAamp contenant le mélange, 500µL de tampon AW1 sera ajouté. Ce mélange sera aussi centrifugé à 8000 tours / minute pendant 1min 30 secondes. Le nouveau tube collecteur sera vidé. Sur la mini colonne QIAamp contenant le mélange, 500µL de tampon AW2 sera ajouté. À cette étape le mélange sera centrifugé à 14000 tours / minute pendant 4 minutes 30 secondes. À la fin de la centrifugation le tube collecteur sera vidé. A la dernière étape, la mini colonne QIAamp contenant l'ADN sera placée sur un tube Eppendorf de 1,5ml préalablement identifié. 100µL de tampon AE sera ajouté pour l'élution de l'ADN. Ensuite la mini colonne QIAamp sera centrifugée à 18000 tours / minutes pendant 2 minutes. L'ADN sera congelé pour conservation.

Dosage de la quantité d'ADN

La quantité de l'ADN pour chaque échantillon extrait sera mesurée à l'aide d'un spectrophotomètre en utilisant un volume de 1µl de l'échantillon avec une longueur d'onde de 230nm.

Evaluation de la qualité de l'ADN : La PCR quantitative

La PCR quantitative (qPCR) sera utilisée pour évaluer la qualité des échantillons extraits. La réaction de qPCR sera réalisée dans un volume final de 20µl à l'aide de QuantStudio™ 3 Real-Time PCR Instrument. Environ 6ng d'ADN seront ajoutés au Mix PCR (10µl de Master Mix 2X Meltdoctor SYBRE Green ; 0,2µl d'amorce sens à 10µM ; 0,2µl d'amorce antisens à 10µM et 8,1µl d'H₂O). Trois gènes contrôles seront amplifiés en utilisant 3 couples d'amorce spécifiques : le gène HPRT (Hypoxanthine Guanine Phosphoribosyl Transférase), le gène ALB (Albumine) et le gène TBP (Tata Box-Binding Protéine). Les réactions d'amplification seront réalisées en triplicat. Le programme thermocycleur sera de 45 cycles : 96°C pendant 15 secondes (séparation des deux brins d'ADN), 60°C pendant 1 minute (hybridation des amorces), 68°C pendant 2 minutes (élongation). Les résultats seront analysés grâce au logiciel QuantStudio™. La taille des amplicons attendue pour

chaque région amplifiée pour les gènes ALB, HPRT et TBP seront de 63pb, 160pb et 295pb respectivement. Pour chaque amplification, une courbe de fluorescence sera tracée par rapport au cycle. La valeur de Ct (Cycle Threshold) sera déterminée dans la phase exponentielle, à l'intersection de la ligne de bruit de fond avec la courbe de fluorescence.

Préparation de librairie pour le séquençage haut débit par CAPTURE

La préparation de librairies sera réalisée à l'aide du kit SOPHIA GENETICS suivant les recommandations du fournisseur par la Plateforme Génétique Moléculaire des Cancers du CHU (PGMC). Le séquençage sera effectué sur le panel GREAT (SOPHIA GENETICS) pour la recherche sur 20 gènes de prédisposition au cancer du sein : ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCA, FANCD2, FANCL, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, RAD54L, TP53.

La réaction de polymérisation en chaîne

Préalablement au séquençage de Sanger et pour confirmer les résultats issus du séquençage NGS, une amplification ciblée par PCR sera réalisée. Les deux régions génomiques d'intérêt seront amplifiées à l'aide de deux couples d'amorces spécifiquement conçus avec le logiciel Primer3 Input (version 0.4.0). Les tailles d'amplicon attendues seront de 225 paires de base (pb) pour le gène TP53 et de 100 pb pour le gène BRCA2. La PCR sera réalisée dans un volume réactionnel final de 50µl. Environ 40ng d'ADN seront ajoutés au mix PCR. Le programme thermocycleur sera réalisé à l'aide du SimpliAmp™ (Applied Biosystems®) suivant : 5min à 94°C, suivi de 35 cycles répétés de 30s à 94°C, 30s à 58°C, 45s à 72°C et une extension finale à 72°C durant 5 minutes. 10µl du produit PCR seront soumis à une électrophorèse sur gel d'agarose à 2% pour vérifier que la taille des amplifications est correcte.

Séquençage de Sanger

Le séquençage sera réalisé après amplification par PCR des régions d'intérêts après purification. Pour cela :

La réaction de purification du produit PCR sera réalisée dans un volume final de 14µl : 10µl produit PCR et de 4µl ExoSapStar™ (Illustra™). Le programme de thermocyclage sera le suivant : 37°C pendant 60 minutes et 80°C durant 15 minutes.

La réaction de séquençage sera réalisée avec l'amorce sens ou antisens : 5µl de mix de séquençage + 1µl d'amorce sens ou antisens à 10µM + 7µl produit du PCR purifié. Le programme de séquençage sera le suivant : 3 min à 94°C, 25 cycles : 96°C pendant 10s, Tm des amorces pendant 5s et 60°C pendant 4min.

Purification de séquence avant injection (Chromatographie d'exclusion) : 400µl de la solution de Séphadex™ G-50 (GE Healthcare) sera ajouté dans les plaques à fond filtrant, centrifuger 3min à 2500rpm ; dépôt de 20µl de séquence au centre sur la colonne puis centrifugation pendant 3min à 2500rpm ; élimination du volume de réaction de séquençage en utilisant un bain marie à sec à une température de 94°C durant 17min, la plaque restera ouverte pour permettre l'évaporation. Reprendre dans 10µl de formamide, dénaturation pendant 3min à 94°C puis la plaque sera placée dans la glace pendant 3min ; transfert des séquences dans la microplaque 96 puits adapté au séquenceur Applied, puis identification et dépôt de la plaque dans le service de séquençage du CHU.

2-Traitement et analyse des données

Les résultats seront saisis sous forme de texte dans le logiciel WORD. Les graphiques seront réalisés dans EXCEL.

3-Considérations éthiques

Le protocole est rédigé en conformité avec les principes généraux d'éthique de la recherche. Sa conduite respectera les recommandations des bonnes pratiques cliniques. La participation à cette étude est volontaire et gratuite. Aucun préjudice supplémentaire ne sera porté au participant du fait de sa participation à l'étude. Les notices d'informations seront remises à chaque participante et son consentement éclairé et signé obtenu avant l'inclusion. Aucune diffusion des données personnelles des participantes n'est possible qu'après l'accord et l'autorisation dûment signée de ceux-ci. Les prélèvements biologiques effectués dans le cadre de cet essai ne seront que strictement utilisés dans cet essai. Aucune manipulation à d'autres fins ne sera possible qu'après l'accord écrit et signé des participants.

Annexe 8: Protocole d'étude sur les réunions de concertation pluridisciplinaire de cancérologie dans les hôpitaux du Bénin : état des lieux et intervention (eRCP).

**LES REUNIONS DE CONCERTATION PLURIDISCIPLINAIRE DE
CANCEROLOGIE DANS LES HÔPITAUX DU BENIN : ETAT DES LIEUX ET
INTERVENTION (eRCP)**

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INTRODUCTION

Le cancer est un problème mondial de santé publique avec des conséquences majeures en termes de morbidité et de mortalité. Selon les données de l'observatoire global sur les cancers GLOBOCAN, l'année 2020 a enregistré près de 19,3 millions de nouveaux cas de cancer et environ 10 millions de décès liés à cette maladie à l'échelle mondiale (Bray et al., 2024). L'Afrique connaît une augmentation préoccupante de l'incidence du cancer. Les chiffres de l'Organisation mondiale de la santé (OMS) indiquent environ 1,3 million de nouveaux cas et 800 000 décès liés au cancer en 2020 sur le continent, des chiffres susceptibles de doubler d'ici 2040 (Sharma et al., 2022). La région subsaharienne supporte une part significative de ce fardeau, avec environ 801 392 nouveaux cas et 520 158 décès liés au cancer en 2020 (Bray et al., 2022). Dans ce contexte, la prévention et la mise en œuvre de stratégies efficaces de prise en charge du cancer deviennent des préoccupations essentielles pour tous les États.

Les réunions de concertation pluridisciplinaires (RCP) ont émergé au début des années 2000 comme des outils cruciaux pour garantir une prise en charge optimale des patients atteints de cancer (Solé, 2018). Ces réunions, rassemblant divers professionnels de santé impliqués dans le traitement du cancer, adoptent une approche multidisciplinaire pour la prise en charge des patients. Elles favorisent la discussion collective, la prise de décisions thérapeutiques basées sur des preuves, et l'élaboration de plans de traitement personnalisés.

Bien que les RCP soient devenues la norme des soins en oncologie dans de nombreux pays développés (Fleissig et al., 2006; Haward, 2006; Institut National du Cancer, 2003), leur utilisation semble être limitée dans les pays en développement (Brandão et al., 2021). Cette situation soulève des interrogations quant à la qualité des décisions prises et à l'équité d'accès aux traitements pour les patients atteints de cancer dans ces pays. Au Bénin, il n'y a pas encore eu à notre connaissance une étude consacrée spécifiquement aux RCP.

Cette étude vise à évaluer la disponibilité des RCP dans les hôpitaux publics béninois et proposer des solutions innovantes.

Problématique

Enoncé du problème

La prise en charge des patients atteints de cancer est devenue de plus en plus complexe, nécessitant une approche multidisciplinaire. Les RCP sont largement reconnues comme la « référence » en matière de soins multidisciplinaires contre le cancer à l'échelle mondiale. En réunissant les professionnels des différentes spécialités impliqués dans la prise en charge du cancer, ces réunions permettent de formuler des recommandations de traitement en tenant compte de l'état de la science et des caractéristiques spécifiques des malades. Des études ont

également montré que cette approche collaborative favorise une meilleure coordination des soins (Ruhstaller et al., 2006), une prise de décision éclairé (Castel et al., 2004; Haddad et al., 2017; Ung et al., 2016) et une amélioration des résultats cliniques pour les patients atteints de cancer (Forrest et al., 2005; Lu et al., 2020; Ray-Coquard et al., 2004).

Dans les pays développés, les RCP sont devenues une pratique courante et bien établie dans la prise en charge des patients atteints de cancer. Plusieurs directives nationales, telles que celles de la France (Institut National du Cancer, 2003), du Royaume-Uni (Fleissig et al., 2006; Haward, 2006), des États-Unis (Tripathy, 2003) et de l'Australie (Luxford & Rainbird, 2001; Zorbas et al., 2003), exigent que tous les cas de cancer soient discutés au sein d'un comité multidisciplinaire. Cependant, dans la plupart des pays à revenu faible ou intermédiaire (PRFI) comme le Bénin, les RCP sont confrontées à de nombreux défis. Une enquête pilote menée en 2013 par Vanderpuye et al. (Vanderpuye et al., 2016), sur la prise en charge du cancer du sein en Afrique au Sud Sahara a révélé que les RCP sont principalement limitées par le manque de médecins spécialisés en oncologie, le faible nombre d'institutions capables d'organiser ces réunions et le manque de soutien gouvernemental.

Toutefois, certains pays d'Afrique au Sud du Sahara font des progrès dans l'organisation de ces réunions, en misant notamment sur les technologies de l'information et de la communication (TIC) (Brandão et al., 2021; Brown et al., 2014; George et al., s. d.; Henderson et al., 2021; Niyibizi et al., 2023). Malgré les défis auxquels ils sont confrontés, des pays à ressources limitées comme le Mozambique sont parvenus à organiser des RCP, ce qui a entraîné une réduction de 53 % de la mortalité liée au cancer du sein (Brandão et al., 2021).

Il est donc crucial de promouvoir davantage les RCP dans ces pays afin de garantir un accès équitable à des soins de qualité. C'est dans cette perspective que s'inscrit cette étude qui vise à évaluer la disponibilité des RCP dans les hôpitaux du Bénin, et identifier les facteurs limitant leur mise en place.

Cadre conceptuel

Une analyse des modèles d'organisation et de fonctionnement des RCP dans les pays développés permet d'identifier plusieurs facteurs pouvant entraver la mise en place de ces réunions dans les pays en développement, tels que le Bénin.

- **Disponibilité des ressources humaines qualifiées en oncologie**

Les ressources humaines formées en oncologie sont extrêmement limitées dans les pays en développement. Une enquête menée en 2006 par la Société Européenne d'Oncologie Médicale, évaluant la situation de la cancérologie dans plusieurs pays en développement, dont le Maroc,

l'Afrique du Sud, la Libye et l'Égypte, a montré qu'il y avait moins de 10 oncologues pour un million d'habitants dans ces pays (Brahmi et al., 2017).

Une enquête plus récente menée en 2013 sur la main-d'œuvre en oncologie clinique dans le monde a révélé un manque en oncologues cliniciens dans les pays en développement (Mathew, 2018). Selon cette enquête, il y avait huit pays où aucun oncologue clinicien n'était disponible pour prodiguer des soins aux patients atteints de cancer. Dans 39 pays, un seul oncologue clinicien devait s'occuper de plus de 500 patients atteints de cancer. Parmi ces pays, 26 étaient en Afrique, soit 81 % de ces pays. La situation était encore plus préoccupante dans certains pays d'Afrique, où une pénurie extrême d'oncologues cliniciens était observée, avec plus de 1.000 cas de cancer par oncologue clinicien. Cette situation concernait 25 pays en Afrique, notamment le Bénin avec 1.250 cas de cancer par oncologue clinicien.

La pénurie en ressources humaines qualifiées en oncologie constitue ainsi un obstacle majeur dans la lutte contre le cancer en général, et dans la mise en place des RCP en particulier. Il convient également de noter que ces ressources sont inégalement réparties, avec une concentration dans les hôpitaux universitaires et dans les zones urbaines. Ceci entraîne des disparités d'accès aux soins pour les patients résidant dans les régions reculées (El Saghir et al., 2015).

▪ **Disponibilité des moyens de diagnostic et de traitement du cancer**

La mise en place des RCP dans les hôpitaux africains est également entravée par le manque d'établissements de santé équipés des moyens diagnostiques et thérapeutiques nécessaires pour étayer les discussions (Vanderpuye et al., 2016). En effet, la plupart des pays africains sont confrontés à des déficits significatifs en matière de services de pathologie et d'imagerie médicale conformes aux normes internationales (Vanderpuye et al., 2016; Ziegenhorn et al., 2020). Ces lacunes dans la disponibilité de ces services engendrent des retards dans la communication des résultats des divers examens, ce qui affecte la prise de décisions appropriées (Vanderpuye et al., 2016).

Par ailleurs, une enquête réalisée en 2010 par l'Agence Internationale de l'Energie Atomique (AIEA), a montré que 29 des 52 pays d'Afrique ne disposent d'aucune installation de radiothérapie, et la majorité des machines existantes se trouvent en Afrique australe et septentrionale (Atun et al., 2015). Une enquête plus récente, menée en 2018 dans 21 pays d'Afrique subsaharienne, a montré que même si la plupart des pays (15/21) disposaient des machines de radiothérapie, celles-ci étaient dans 22 % des cas en panne. Par exemple en 2008, la Tanzanie, ne disposait que de deux appareils de radiothérapie pour un besoin réel de 45

appareils (Hanna & Kangolle, 2010). Il n'y avait que trois unités de mammographie, cinq tomodensitomètres et un appareil d'IRM, ce qui limitait les capacités de dépistage et de stadification des cancers. La situation est encore plus préoccupante dans d'autres pays comme le Bénin, qui jusqu'en 2023, ne dispose pas d'unité de radiothérapie fonctionnelle.

- **Disponibilité d'un cadre institutionnel ou réglementaire encadrant les RCP**

La disponibilité d'un cadre institutionnel encadrant et incitant l'organisation des RCP est l'une des principales raisons expliquant un meilleur développement de ces réunions dans les pays développés par rapport aux pays en développement. Au Royaume-Uni, par exemple, la refonte des services de cancérologie et l'adoption rapide des RCP au cours des dernières décennies ont été principalement motivées par la pression politique résultant d'une série de rapports publiés à la fin des années 1990 (Fleissig et al., 2006; Haward, 2006). Une fois que les décideurs politiques ont reconnu la valeur clinique d'une approche de gestion des maladies en équipe multidisciplinaire, celle-ci est devenue la norme de soins dans la plupart des systèmes de santé modernes (Cawich et al., 2014).

Dans la plupart des pays développés, des "Plans Cancer" conçus pour définir la politique nationale de lutte contre le cancer régissent également les modes d'organisation et de fonctionnement des RCP. Ces réunions bénéficient même d'un soutien financier qui facilite leur implémentation (De Ieso et al., 2013). En revanche, l'engagement des politiques dans la lutte contre le cancer est moins prononcé dans les pays en développement (Pezzatini et al., 2007). Les ressources limitées, les priorités concurrentes en matière de santé et les infrastructures de santé fragiles peuvent rendre difficile l'adoption et la mise en œuvre de politiques spécifiques pour les RCP. De plus, le manque de sensibilisation et de compréhension de l'importance de ces réunions peut également constituer un obstacle à leur développement dans ces pays.

À titre illustratif, l'analyse menée en 2021 par Khiari et al. sur les stratégies de prise en charge des cancers dans les pays du Maghreb (Tunisie, Maroc et Algérie) a révélé que bien que ces pays aient tous adopté un plan national de lutte contre le cancer, ces plans n'ont pu être mis en œuvre, en raison d'un sous-financement, associé à un manque d'engagement des parties prenantes (Khiari et al., 2021).

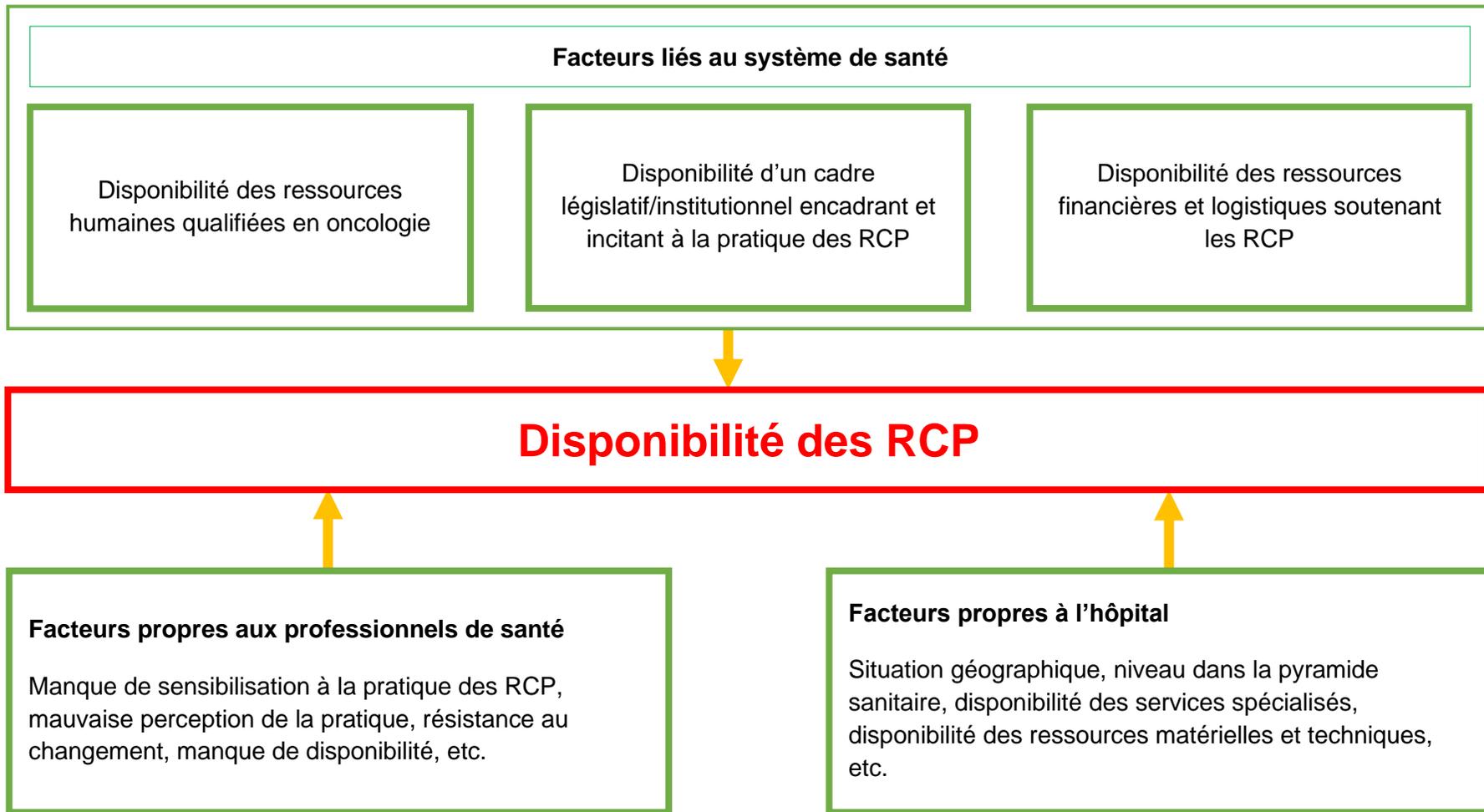


Figure 9 : Cadre conceptuel montrant les facteurs associés à la disponibilité des RCP dans les pays en développement

Légende :



: variable dépendante



: variable indépendante



: décrit la relation entre variable dépendante et variable indépendante

L'objectif principal de cette étude est de contribuer à l'amélioration de la disponibilité des RCP de cancérologie dans les hôpitaux du Bénin.

Objectifs spécifiques

Plus spécifiquement, il s'agit de :

- Faire un état des lieux de la disponibilité des RCP dans les hôpitaux du Bénin.
- Identifier les obstacles liés à la mise en place et à la tenue des RCP dans les hôpitaux du Bénin.
- Concevoir une solution technologique dédiée à l'organisation et à la gestion des RCP dans les hôpitaux du Bénin et les hôpitaux d'ASS plus généralement.

Méthodologie de la recherche

Cette étude se déroulera en trois phases :

1. Une enquête de terrain pour évaluer la disponibilité des RCP dans les hôpitaux du Bénin et évaluer les besoins spécifiques des professionnels de santé
2. La conception et l'implémentation d'une plateforme de RCP virtuelle (eRCP) répondant aux besoins identifiés
3. Évaluation de la plateforme basée sur les retours des professionnels de santé.

Enquête de terrain

▪ **Type d'étude**

Il s'agira d'une étude transversale à visée descriptive et analytique, avec collecte prospective des données sur une période de deux (02) mois.

▪ **Population d'étude**

La population d'étude pour cette recherche sera constituée des hôpitaux du Bénin, susceptibles de prendre en charge les patients atteints de cancer, ainsi que leur personnel médical.

● **Sélection des hôpitaux**

Il sera procédé à un recrutement exhaustif de :

- tous les hôpitaux publics, privés ou confessionnels situés sur le territoire national ;
- susceptibles de prendre en charge les cas de cancer.

● **Sélection des participants**

Après le recrutement des hôpitaux, un tirage au sort sera effectué pour sélectionner de façon aléatoire un professionnel de santé dans chaque établissement de santé. Le tirage au sort sera effectué parmi les responsables des services susceptibles de prendre en charge les cas de cancer :

- service de cancérologie,
- service de chirurgie,
- service de gynécologie-obstétrique,
- service de médecine interne,
- service de gastro-entérologie,
- service de médecine ou de médecine générale,
- service d'imagerie médicale,

- service d'anatomie pathologique.

En cas de non-disponibilité (professionnel injoignable après trois relances espacées de 48 heures) ou de refus de participation, un autre professionnel sera tiré au sort. Le tirage au sort sera effectué à l'aide d'un programme Python spécialement conçu.

▪ **Collecte de données**

Les données seront recueillies à l'aide d'un questionnaire structuré renseignant sur :

- la disponibilité des ressources pour le diagnostic et le traitement du cancer,
- la présence des RCP pour la prise en charge des patients atteints de cancer,
- les modalités d'organisation et de fonctionnement des RCP,
- les défis liés à l'organisation et à la participation aux RCP,
- la perception des professionnels de santé vis-à-vis des RCP,
- et la faisabilité d'organiser des RCP virtuelles.

Le questionnaire sera accessible en ligne via la plateforme Microsoft Team pour permettre aux participants de répondre aux questions à leur propre rythme.

- **Variables d'étude**
- **Variable dépendante**

La variable dépendante de cette étude sera la disponibilité des réunions de concertation pluridisciplinaire (RCP) dans les hôpitaux du Bénin. L'opérationnalisation de cette variable prend en compte les aspects suivants :

- La **disponibilité des RCP** : Pour évaluer la disponibilité des RCP dans chaque hôpital inclus dans l'étude, une échelle binaire sera utilisée. Elle présentera deux modalités : oui et non.
- La **fréquence des RCP** : La fréquence à laquelle sont organisées les RCP sera quantifiée pour chaque hôpital.
- La **multidisciplinarité des RCP** : L'évaluation de la participation des différents professionnels de santé lors des RCP.

- **Variables indépendantes**
 - **Caractéristiques des hôpitaux**
 - **Localisation géographique** : département de localisation de l'hôpital
 - **Niveau de l'hôpital** :
 - Hôpital National
 - Centre Hospitalier Départemental
 - Hôpital de Zone
 - Hôpital Universitaire
 - **Disponibilité des ressources pour le diagnostic et le traitement du cancer**
 - **Caractéristiques du personnel de santé**
 - Grade/ ancienneté
 - Spécialité
 - Perception vis-à-vis des RCP
 - **Facteurs organisationnels**
 - Disponibilité des ressources humaines dédiées aux RCP
 - Existence d'une charte ou d'un manuel de procédure des RCP
 - Utilisation d'outils technologiques pour l'organisation et la gestion des RCP

- **Traitement et analyse des années**

Les données collectées seront importées dans une base Excel puis nettoyées et codifiées. L'analyse des données sera effectuée à l'aide du logiciel R. Les variables quantitatives seront présentées sous forme de moyenne accompagnée de l'écart-type ou de la médiane avec intervalle interquartile, selon leur distribution. Les variables qualitatives seront exprimées en nombre d'occurrences et en pourcentage.

Pour évaluer l'association entre les variables indépendantes et la variable dépendante (disponibilité des RCP), des analyses de régression bivariée et multivariée seront menées. L'association entre les facteurs identifiés et la variable d'intérêt sera évaluée à l'aide de l'odds ratio (OR) et de son intervalle de confiance à 95% (IC95%). Un seuil de significativité de 5% ($p\text{-value} < 0,05$) sera retenu.

- **Conception et implémentation d'une plateforme virtuelle pour les RCP (eRCP)**
- **Conception de la Plateforme**

La plateforme eRCP sera conçue en tenant compte des résultats de l'enquête de terrain. Elle visera à faciliter l'organisation et la gestion des RCP, en offrant des fonctionnalités adaptées aux besoins spécifiques des professionnels de santé.

Elle consistera en la numérisation et la sécurisation du processus des Réunions de Concertation Pluridisciplinaire (RCP) en cancérologie. Elle proposera une plateforme centralisée permettant la collaboration entre les médecins pour proposer des solutions optimales aux patients atteints du cancer. Elle reposera sur des technologies modernes de communication et de sécurité de données ; ce qui permettra de répondre efficacement à la question de la sécurité des données médicales.

- **Résultats et bénéfices attendus**

Les résultats attendus de cette solution informatique sont les suivants :

- **Centralisation et collaboration** : La plateforme offrira un espace centralisé pour la gestion des RCP, facilitant ainsi la collaboration et la communication entre les médecins spécialistes,
- **Sécurité des données** : Les données médicales seront sécurisées grâce à des protocoles de chiffrement avancés, assurant la confidentialité et l'intégrité des informations.
- **Accessibilité à distance** : Les médecins pourront participer aux RCP à distance, éliminant les barrières géographiques et améliorant la prise en charge des patients atteints du cancer situés dans les localités les plus démunies.
- **Meilleure prise en charge des patients** : Une gestion plus efficace des RCP permet une prise en charge plus rapide et coordonnée des patients atteints de cancer.
- **Amélioration des pratiques médicales** et formation continue y compris pour les praticiens des zones rurales: L'intégration de la technologie dans le domaine médical renforce les pratiques professionnelles et la qualité des soins.
- **Recherches scientifiques en cancérologie** : L'utilisation de l'innovation eRCP va permettre la constitution de bases de données médicales qui va ouvrir d'autres perspectives de recherches scientifiques en cancérologie.

▪ **Procédure d'Implémentation**

- Sélection des participants : tous les professionnels de santé recrutés lors de la première phase, ainsi que les médecins et professionnels de Santé des hôpitaux participants, désireux de présenter des cas de patients atteints de cancer, pourront participer à l'implémentation.
- Formation : Les participants seront formés à l'utilisation de la plateforme, en mettant l'accent sur la navigation, la soumission de cas, et les différentes fonctionnalités.

Évaluation de la plateforme

La plateforme sera évaluée en tenant compte des retours des participants. Trois séances tests seront organisées pour permettre aux participants d'expérimenter la plateforme dans des conditions réelles. Après chaque séance, un questionnaire sera adressé aux participants pour recueillir leurs témoignages et leurs perceptions quant à la facilité d'utilisation, l'utilité perçue et les suggestions d'amélioration.

Perspectives de développement de l'intervention proposée

L'innovation eRCP offrira des perspectives de développement continues, notamment :

- **Extension** à d'autres domaines et pays de la sous-région : possibilité d'adapter la plateforme à d'autres domaines médicaux nécessitant des réunions multidisciplinaires et à d'autres pays de la sous-région qui connaissent des difficultés dans la prise en charge efficiente des patients atteints du cancer.
- **Collaboration avec les médecins à l'étranger** : Ouvrir la plateforme eRCP aux médecins étrangers et de la diaspora. En effet, le Bénin comme de nombreux pays de d'ASS disposent de médecins hautement qualifiés dans leur diaspora ; et qui sont motivés pour appuyer les équipes locales notamment lorsque ces compétences techniques ne sont pas disponibles dans les pays d'origine.
- **Développement d'une version mobile de eRCP** : Mise en place d'une version mobile de la plateforme eRCP afin que les médecins puissent aisément participer aux réunions même lorsqu'ils sont en déplacement.
- **Automatisation du processus de décision** : Ajout de l'IA pour explorer les possibilités de la décision basée sur l'apprentissage automatique.

- **Collaborations internationales** : Possibilité de collaborer avec d'autres institutions médicales à l'échelle internationale pour partager les bonnes pratiques et améliorer la gestion des cas complexes. Par exemple réalisation de **RCP intercontinentales** avec des spécialistes des centres de référence à l'échelle internationale.

Considérations éthiques

Le protocole est rédigé en conformité avec les principes généraux d'éthique de la recherche clinique (Helsinki 1964 et ses versions successives modifiées). Il sera soumis au comité d'éthique des recherches en sciences de la santé.

La participation à cette étude sera volontaire et gratuite. Le libre consentement des professionnels de santé et l'anonymat des informations recueillies seront également respectés. Conformément au principe du secret professionnel, la confidentialité sera rigoureusement respectée lors de l'enquête.

A la fin de l'étude, les données seront conservées pendant une durée minimale de quinze (15) ans. Les résultats de l'étude seront partagés avec les participants et le Ministère de la Santé de la République du Bénin.

Budget

Budget développement, tests et mise en phase pilote (production) de la plateforme e-RCP (euro)					
Désignation	Descriptif sommaire	Unité	Prix Unitaire	Quantité	Montant
Conception et développement de la plateforme	la concetion et le développement fera appel aux compétences d'une équipe pluridisciplaine composée de : 1 Architecte système chef de projet 1 designer UX 1 développeur front-end 2 développeurs back-end 1 spécialiste en sécurité des applications 1 programmeur ayant un background en data science	Ff	7616,66	1	7617
Achat de licence de solutions de visioconférence	Achat de licences de la solution de visioconférence qui permet de lancer les appels	U	304,67	1	305
Achat d'un domaine .bj pour la plateforme		U	30,47	1	30
Hébergement de la solution pour la première année		U	121,87	1	122
Achat d'un certificat SSL pour la sécurité des informations qui transitent sur le site		U	152,33	1	153
Renouvellement du domaine et de l'hébergement de la solution chaque année		U	152,33	1	153
Renouvellement de la licence de la soution de visioconfrérence		U	152,33	1	153
Renouvellement de la licence du certificat de sécurité SSL		U	152,33	1	153
Maintenance régulière de la plateforme sur 1 an (curative et évolutive)		ff	3046,67	1	3047
Total					11 886

Annexe 9: Fiche d'enquête (étude épidémiologique des cancers du sein en population générale à partir des données du registre des cancers de Cotonou de 2014-2019).

FICHE D'ENQUETE

N° de la fiche :.....

Hôpital : /___/ CNHU=1 CHU-MEL= 2

Service : /___/ CUGO=1 Viscéral=2

N° du dossier : /_____/

N° de téléphone :

Date d'admission ou de la 1^{ère} consultation :

I- RENSEIGNEMENTS SOCIODEMOGRAPHIQUES DE LA PATIENTE

Nom :.....

Prénoms :

Age : (en année) :

Age au moment du diagnostic

Profession : /___/

Elève=1 Etudiante=2 Sans emploi=3 Ménagère=4 Agent d'exécution=5

Artisan/travailleur=6 Commerçant=7 Agent de santé=8

Niveau d'instruction : /___/

Sans instruction =1 Niveau primaire=2 Niveau secondaire=3 Supérieur=4

Zone de résidence : /___/

Urbain=1 Rural=2

Ethnie : /___/

Fon=1 Mina=2 Dendi=3 Bariba=4 Goun=5 Yoruba/Nagot=6 Adja=7 Autres

africains=8

Religion : /___/

Catholique=1 Evangélique=2 Musulmane=3 Christianisme Céleste = 4

Animiste = 5 Athée=6

II- DONNEES RELATIVES AU CONJOINT :

Nom :.....

Prénoms :.....

Age : (en année) :.....

Profession : /___/

Elève=1 Etudiante=2 Sans emploi=3 Ménagère=4 Agent d'exécution=5
Artisan/travailleur=6 Commerçant=7 Agent de santé=8

Régime matrimonial : /___/

Monogamie=1 Polygamie= 2

III- Eléments du diagnostic

1- Motif de consultation : /___/

Inflammation=1 Nodule=2 Mastodynie=3 Ecoulement mamelonnaire=4 Ulcération cutanée=5
Lymphoedème=6 Syndrome para néoplasique=7 Métastases=8 Adénopathies= 9

2- Délai de consultation (mois) : /___/

3- Signes cliniques

Etat général initial : IP/OMS : /___/

Poids (kgs)= /___/

Taille (cm)= /___/

Maigrissement >10% : /___/ Oui=1 Non=2

Caractéristiques de la tumeur

Latéralité du sein : /___/ Droit=1 Gauche=2

Quadrant : /___/ Inféro interne=1, Inféro externe=2, Supéro-interne=3, Supéro-externe=4

Taille de la lésion primitive : /___/ (cm)

Classification c TNM

Taille de la tumeur(T) : /___/ T0=0 T1=1 T2=2 T3= 3 T4=4 Tx=5

Ganglions régionaux (N) : /___/ N0=0 N1=1 N2=2 N3=3 Nx=4

Métastases (M) : /___/ M0=0 M1=1 Mx=2

Stade UICC : /___/ Stade 0=0 Stade I=1 Stade II=2 Stade III= 3 Stade IV= 4

Si métastases (lors du diagnostic), localisation : /___/

Cerveau=1 Poumon=2 Foie=3 Os=4 Autres= 5 (Préciser)

4- Données paracliniques

Mammographie :

Classification ACR : /___/ ACR0=0 ACR1=1 ACR2= 2 ACR3=3 ACR4=4

ACR5=5

Taille des lésions : /___/ (mm)

Echographie :

Classification ACR: /___/ ACR0=0 ACR1=1 ACR2= 2 ACR3=3 ACR4=4

ACR5=5

Adénopathies suspectes à l'échographie : /___/ Oui=1 Non=2

Si oui, préciser Siege : /___/ Cervicale=1 Thoracique=2 Abdominale=3

Pelvienne=4

Type de biopsie :

Cytoponction à l'aiguille fine : /___/ Oui=1 Non=2

Si oui, résultats : /___/ Positif=1 Négatif=2

Biopsie à l'aiguille true cut : /___/ Oui=1 Non=2

Histologie :

Type de prélèvement : /___/ Biopsie=1 Pièce opératoire=2 Nodules= 3

Echoguidée : /___/ Oui =1 Non=2

Examen extemporané : /___/ Oui =1 Non=2

Taille de la tumeur : /___/ (mm)

Type histologique : /___/

C. canalaire in situ=1 C.lobulaire in situ=2 C. canalaire infiltrant(NS)=3 C.

lobulaire infiltrant=4 C.tubuleux=5 C.médullaires=6 C.mucineux=7

C.adénoïdes kystiques ou cylindromes=8 C.métaplastique=9 C.

inflammatoires=10 Autres tumeurs malignes non épithéliales=11

- Classification SBR : /___/ SBR1=1 SBR2=2 SBR3=3 Inconnu=4

- Immunohistochimie

Récepteurs aux œstrogènes : /___/ (+)=1 (-)=2

Taux : /___/ Intensité : /___/ Une croix=1 Deux croix=2 Trois croix=3

Récepteurs à la progestérone : /___/ (+)=1 (-)=2

Taux : /___/ Intensité : /___/ Une croix=1 Deux croix=2 Trois croix=3

HER2 : /___/ Absent = 0 Une croix=1 Deux croix=2 Trois croix=3

Profil IHC : /___/

Luminal A =1, Luminal B non Her=2, Luminal B, Her=3 HER2=4,
Triple Négatif =5, Inclassable=6

Bilan d'extension

Scanner thoraco abdomino pelvien

Si métastases, localisation : /___/

Cerveau=1 Poumon=2 Foie=3 Os=4 Autres= 5 (Préciser)

Echographie abdomino pelvienne

Si métastases, localisation : /___/

Foie=1 Autres= 2 (Préciser)

Radiographie pulmonaire

Si métastases, localisation : /___/

Poumon=1 Autres= 2 (Préciser)

IRM

Si métastases, localisation : /___/

Cerveau=1 Poumon=2 Foie=3 Os=4 Autres= 5 (Préciser)

Biologie

Marqueur CA15-3(pré thérapeutique) : /___/ Oui=1 Non=2 Valeur/___/

5-Modalités du traitement

Chimiothérapie :

Indiquée : /___/ Oui=1 Non=2

Si oui, type de chimiothérapie : /___/ Adjuvante=1 Néo adjuvante=2 Palliative=3

Nombres de lignes : /___/

Ligne numéro 1

Protocole: /___/

AC-Taxotere=1 EC-Taxotere=2 EC-Taxol=3 AC-Taxol=4 Taxol=5 Taxotere=6 Navelbine=7

Carboplatine=8 Autres=9

Nombre de cycles : /___/

Réponse /___/ Oui=1 Non=2

Ligne numéro 2

Protocole : /___/

AC-Taxotere=1 EC-Taxotere=2 EC-Taxol=3 AC-Taxol=4 Taxol=5 Taxotere=6 Navelbine=7
Carboplatine=8 Autres=9

Nombre de cycles : /___/

Réponse /___/ Oui=1 Non=2

Ligne numéro 3

Protocole: /___/

AC-Taxotere=1 EC-Taxotere=2 EC-Taxol=3 AC-Taxol=4 Taxol=5 Taxotere=6 Navelbine=7
Carboplatine=8 Autres=9

Nombre de cycles : /___/

Réponse /___/ Oui=1 Non=2

Chirurgie :

Indiquée : /___/ Oui=1 Non=2

Faite : /___/ Oui=1 Non=2

Objectif de la chirurgie : /___/ Palliatif=1 Curatif=2

Refus du traitement/___/ Oui=1 Non=2 si Non

Type de chirurgie : /___/ Radicale=1 Conservatrice=2

Si Radicale, type de Mastectomie réalisée : /___/ Patey modifié Madden=1 Halsted=2

Mastectomie simple=3

Si Conservatrice : /___/ Quadrantectomie=1 Tumorectomie=2

Délai de la chirurgie : /___/ (mois)

Curage axillaire : /___/ Oui=1 Non=2

Biopsie du ganglion sentinelle : /___/ Oui=1 Non=2

Dissection de ganglion axillaire : /___/ Oui=1 Non=2

Complications : /___/ Oui=1 Non=2

Si Oui type de complications : /___/ Hématome=1 Abscès=2 Lymphoedème=3 Lymphocèle=4

Limitation du membre =5

Durée d'hospitalisation après chirurgie : /___/

Classification p TNM après chirurgie et anatomie pathologie

Taille de la tumeur : /___/ mm

Nombre de ganglions envahis : /___/

Nombre total de ganglions dans la pièce opératoire : /___/

Tumeur(T) : /___/ T0=0 T1=1 T2=2 T3= 3 T4=4 Tx=5

Ganglions régionaux (N) : /___/ N0=0 N1=1 N2=2 N3=3 Nx=4

Radiothérapie :

Indiquée : /___/ Oui=1 Non=2

Faite : /___/ Oui=1 Non=2

Délai par rapport à la chirurgie : /___/ (mois)

Prise en charge : /___/ Etat=1 Patient=2 Assurance=3

Lieu d'évacuation : /___/ Afrique de l'ouest=1 Afrique du Nord =2 Europe=3 Autres=5

Hormonothérapie

Indiquée : /___/ Oui=1 Non=2

Faite : /___/ Oui=1 Non=2

Molécule : /___/ Tamoxifène=1 Anti-aromatases=2 Autres=3 Préciser

Thérapie ciblée

Indiquée : /___/ Oui=1 Non=2

Faite : /___/ Oui=1 Non=2

Si oui, type : /___/ Adjuvante=1 Néo adjuvante=2 Palliative=3

Molécule : /___/ Trastuzumab=1 Pertuzumab=2 Autres=3 (préciser)

6-Evolution

Evolution : /___/

Rémission complète=1 Perte de vue=2 Récidive=3 Décédé=4

Si décès, cause : /___/ Cancer=1 Autre=2

Durée de suivi : /___/ (mois)

Récidive : /___/ Oui=1 Non=2

Si Oui délai : /___/ (mois)

Type de récurrence : /___/ Locale=1 Régionale=2 Locorégionale=3 Métastases=4

Si métastases, localisation : /___/

Cerveau=1 Poumon=2 Foie=3 Os=4 Autres=5 (préciser).....

Survie à 5 ans : /___/

Décès =1, vivante = 2

Contribution à la connaissance du fardeau et des facteurs pronostiques du cancer du sein au Bénin et en Afrique au Sud du Sahara

La thèse aborde de manière approfondie le fardeau et les facteurs pronostiques du cancer du sein au Bénin et en Afrique au Sud du Sahara (ASS). Tout d'abord, elle révèle une prévalence alarmante de diagnostics à des stades tardifs et des formes cliniques de pronostic péjoratif. Cette constatation souligne l'urgence d'améliorer les stratégies de dépistage et d'accès aux traitements systémiques et à la radiothérapie pour permettre un diagnostic précoce et une prise en charge efficace. En outre, l'étude évalue la coordination des soins dans un contexte où les ressources humaines et matérielles sont souvent limitées. Les résultats révèlent des lacunes dans la coordination des soins et la capacité des systèmes de santé à assurer le continuum des soins pour les patientes ; soulignant la nécessité de renforcer les capacités des professionnels de la santé et d'améliorer les programmes de navigation du patient. En prenant des mesures concrètes pour répondre à ces défis, il est possible d'espérer une amélioration significative des résultats cliniques et une réduction du fardeau du cancer du sein pour les femmes au Bénin et en Afrique au Sud du Sahara plus généralement.

Mots-clés : Cancer du sein, Epidémiologie, fardeau, Incidence, Mortalité, Facteurs pronostiques, Hôpitaux, Systèmes de santé, Prévention, Politiques, République du Bénin, Afrique au Sud du Sahara.

Contribution to understanding the burden and prognostic factors of breast cancer in Benin and Sub-Saharan Africa

The thesis extensively addresses the burden and prognostic factors of breast cancer in Benin and Sub-Saharan Africa (SSA). Firstly, it unveils an alarming prevalence of late-stage diagnoses and clinically unfavorable prognostic forms. This observation underscores the urgent need to enhance screening strategies and access to systemic treatments and radiotherapy to enable early diagnosis and effective management. Furthermore, the study evaluates care coordination in a context where human and material resources are often limited. The results reveal shortcomings in care coordination and the healthcare system's capacity to ensure continuum of care for patients, underscoring the necessity to strengthen healthcare professionals' capacities and improve patient navigation programs. By implementing concrete measures to address these challenges, there is potential for significant improvement in clinical outcomes and a reduction in the burden of breast cancer for women in Benin and Sub-Saharan Africa more broadly.

Keywords: Breast Cancer, Epidemiology, Burden, Incidence, Mortality, Prognostic Factors, Hospitals, Healthcare Systems, Prevention, Policies, Republic of Benin, Sub-Saharan Africa.

