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Research article

Projection of morbidity and mortality due to breast cancer between 2020 and 2050 across 42 low- and middle-income countries

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ABSTRACT

Objective: Aim of the study is to predict trends in morbidity and mortality due to breast cancer in 42 LMICs between 2020 and 2050.
Design: and Setting: National level cross-sectional breast cancer related data between 1990 and 2019 were used. Recurrent Neural Network, Long-Short-Term Memory (RNN-LSTM) model was employed to forecast the trend in breast cancer burden.
Main outcomes and measures: Age standardized breast cancer incidence, mortality, and disability adjusted life years (DALYs) rates.
Results: By 2050, the age standardized breast cancer incidence rate is expected to increase in 38 LMICs with highest incidence rate in Namibia; 127.0 (78.0–176.0) followed by Nigeria 71.1 (53.9–88.3) and Papua New Guinea 70.6 (88.7–74.6). Similarly, the age standardized breast cancer mortality and DALYs rates in 2050 are expected to increase in 33 and 35 LMICs respectively. The highest mortality and DALYs rates in 2050 are expected to be 64.7 (42.6–86.7) in Namibia and 1543.6 (1463.1–1624.1) in Pakistan. The estimated annual percentage change (EAPC) is expected to increase uniformly in all the countries during the same period. Due to considerable variation in exposure risk, such as high plasma glucose level, high body mass index (BMI) and socio-demographic index (SDI), high regional disparity in burden of breast cancer is expected among the countries.
Conclusion: and Relevance: Breast cancer burden is expected to increase in most of the LMICs with high regional disparity by 2050. Our study's finding focuses on LMICs with high breast cancer burden that require tailored strategies and effective action plans to ensure prevention from catastrophic consequences in the future. Minimizing the exposure to behavioral and metabolic risk factors such as high plasma glucose, high BMI, along with tackling the issue of low fertility rate would be important in managing breast cancer burden in LMICs.

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1. Introduction

The burden of breast cancer is rising significantly in low-and middle-income countries (LMICs). The epidemiologic trend of breast cancer is of particular concern as it has surpassed the lung cancer as most commonly diagnosed cancer globally [1,2]. Breast cancer incidence rate is in increasing trend in many LMICs even though the absolute incidence is lower in those countries compared to that in high-income countries (HICs) [3,4]. For instance, between 2000 and 2020 the breast cancer incidence rate in HIC increased by 35% whereas in LMICs it has doubled during the same time period [5,6]. Unlike in HICs, where breast cancer mortality rate is in decreasing trend, it has been increasing rapidly in LMICs [1,3].

The rising burden of breast cancer along with other forms of cancer has strained the limited health care and economic infrastructure in LMICs and poses a huge socioeconomic challenge [7]. Previously conducted studies showed that the year of productive life loss (YPLL) and gross domestic product (GDP) loss due to breast cancer in LMICs particularly in Sub-Saharan Africa and South Asia is significantly high. In Sub- Saharan Africa and South Asia, 0.082% GDP loss was accounted because of breast cancer during 2005–2015 [7]. On March 8, 2021, WHO, in collaboration with International Agency for Research on Cancer (IARC), and the International Atomic Energy Agency (IAEA) initiated Global Breast Cancer Initiative (GBCI) with one of the major objectives to reduce global breast cancer mortality by 2.5% per year, thereby averting 2.5 million breast cancer related deaths globally between 2020 and 2040 [8]. Achieving the objective set by GCBI to successfully reduce the burden of breast cancer in LMICs, it is essential to have concrete evidence about breast cancer burden in LMICs including the estimation of future pattern and trend in breast cancer incidence, mortality, and disability adjusted life years (DALYs) rates. Therefore, the aim of the study is to analyze the existing burden of breast cancer as well as associated risk factors in 42 LMICs by forecasting the trend in age standardized breast cancer incidence, mortality, and DALYs rates between 2020 and 2050.

2. Methods

In this study, we used national level estimates of age standardized breast cancer incidence, mortality and DALYs rates along with breast cancer risk factors estimates between 2020 and 2050. After a thorough literature review and exploration of data availability, we selected 42 LMICs from Global Health Data Exchange (GHDx), Institute for Health Metrics and Evaluation (IHME) [9]. List of 42 LMICs by regional classification is provided in the Supplementary Table 1. Global Burden of Diseases is the most comprehensive global epidemiological study initiated by IHME at the University of Washington [10–12]. The details of data source are provided elsewhere [9,13]. In the latest GBD study (covering up to the year 2019), age standardization was performed by direct method, applying the global age structure from 2019. In addition, we predicted global level average age standardized breast cancer incidence, mortality, and DALYs rates between 2020 and 2050 using global average estimates between 1990 and 2019 from GHDx.

The major outcome variables included in this study were age standardized breast cancer incidence, mortality, and DALYs rates per 100,000 population between 2020 and 2050. The predictor variables of age standardized breast cancer were selected by a thorough literature review on PubMed using terms such as risk factors OR predictors OR exposure risks of breast cancer. Five major behavioral and metabolic risk factors and three sociodemographic and economic factors were selected for the prediction model. After the model training three major factors, high plasma glucose level, high body mass index (BMI) and socio-demographic index (SDI) were included in the final prediction model. The definitions of the outcome variables and breast cancer risk factors are provided in the supplementary material.

In addition, we predicted global level average estimate for age standardized breast cancer incidence, mortality, and DALYs rates between 2020 and 2050 as a reference to interpret national level estimates of 42 LMICs.

3. Human participants

This study does not involve human participants.

3.1. Patient and public involvement

No patients/public were involved in the design of the study. No patients were involved in the recruitment to conduct the study.

4. Statistical analyses

4.1. Prediction using bidirectional Long Short-Term Memory (LSTM) model

We used bidirectional Long Short-Term Memory (LSTM) model, a variant of Recurrent Neural Network (RNN) model in Deep learning technique to predict the trend in age-standardized breast cancer incidence, mortality, and DALYs rates between 2020 and 2050. Unlike conventional statistical time series prediction models, deep learning models, such as bidirectional LSTM, allow intricate non-linear procedures without difficulty. Bidirectional LSTM model can process long term temporal data and time series predictions without losing prior information over time [14,15]. The model processes inputs in both direction forward (future direction) and backward (past direction), that utilizes information from both sides with long term temporal dependencies (Supp. figure 1), [16]. Further explanation of LSTM model and its advantages over traditional time series models is provided in appendix.

The bidirectional LSTM model used in our study comprised of an input layer, one hidden LSTM layer with 100 dimensions, and an

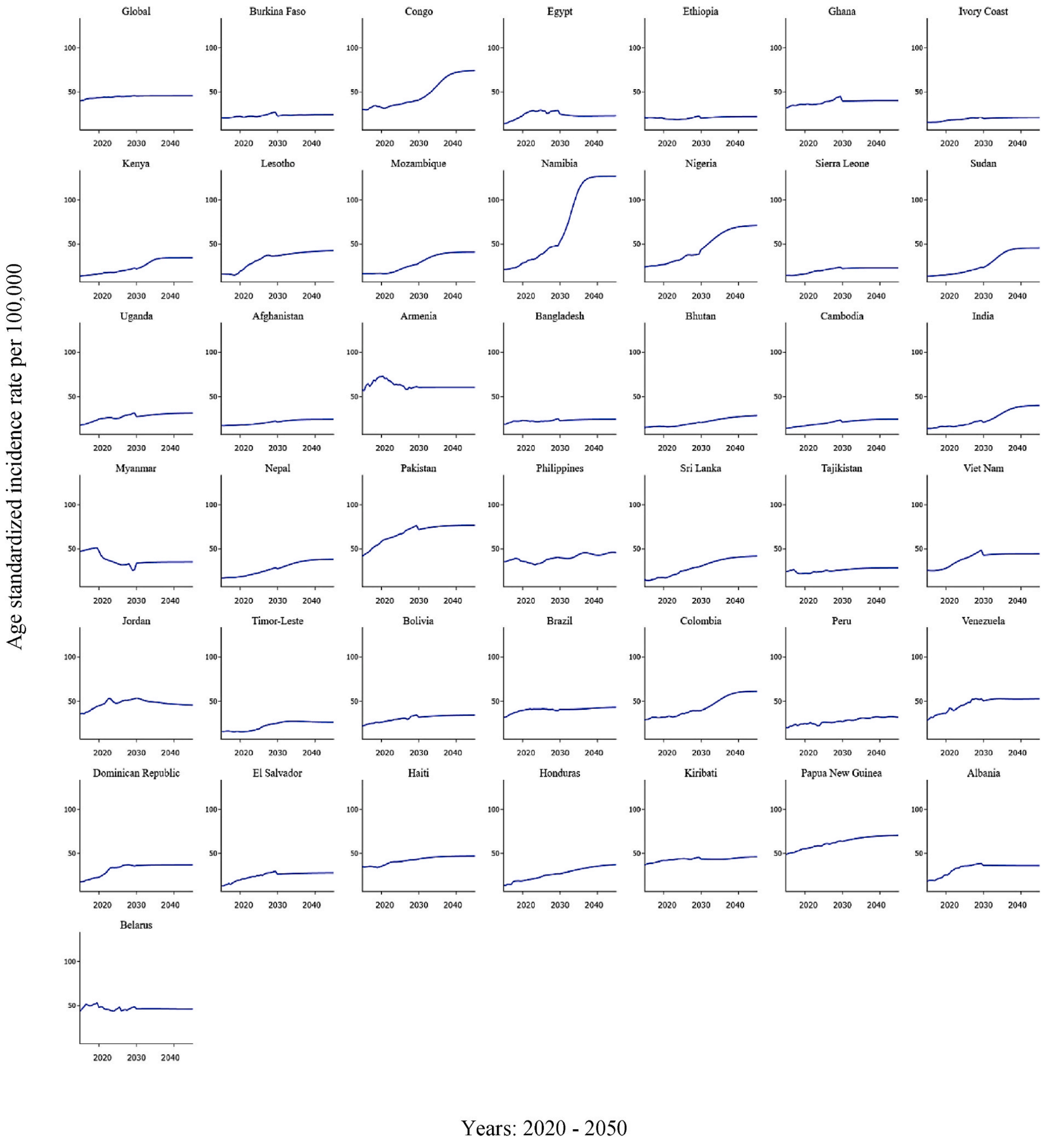


Fig. 1. Projected trend in age standardized breast cancer incidence rate between 2020 and 2050. *Incidence rate has been age standardized.

output layer. Breast cancer risk factors data such as high plasma blood glucose, high body mass index, and socio-demographic were fed to the model as inputs along with the estimates of breast cancer incidence, mortality, and DALYs rates between 1990 and 2019. The pre-processed data between 1990 and 2019 was split into training and testing datasets in 80:20 ratio. Furthermore, one third of the testing dataset was segregated into a validation dataset. The optimization of hyperparameter was done by grid search technique on training and validation set. Details of bidirectional LSTM model are presented in Table 1.

4.2. Estimated annual percentage change (EAPC)

To measure the trend in age standardized breast cancer incidence, mortality, and DALYs rates estimated annual percentage change (EAPC) was calculated. EAPC is a measure of the age standardized rates ASR trend over a time interval using generalized linear model

Table 1
Summary of bidirectional LSTM model along with hyperparameter optimization.

Hyperparameters	Selection
LSTM layers	Single layer
Optimizer	Adam optimizer
Activation function	Hyperbolic Tangent
Number of input features	4
Number of epochs	100
Loss function	Root Mean squared error (RMSE)
Batch Size	32
Dropout	20%
Normalization	MinMax scaler

*Number of epochs, batch size, dropouts were determined through optimization of hyper parameter using GridsearchCV.

Table 2
EAPC in age standardized breast cancer incidence, mortality, and DALYs rates between 2020 and 2050.

Country	EAPC in incidence rate (%, 95% CI)	EAPC in mortality rate (%, 95% CI)	EAPC in DALYs rate (%, 95% CI)
Africa			
Global	0.02 (−0.56 to 0.60)	0.01 (−0.98 to 1.01)	0.09 (−0.09 to 0.27)
Burkina Faso	0.17 (−0.63 to 0.98)	0.13 (−0.78 to 1.04)	0.05 (−0.13 to 0.23)
Congo	2.02 (1.51 to 2.53)	−0.07 (−0.81 to 0.67)	0.53 (0.40 to 0.66)
Egypt	−0.16 (−0.97 to 0.66)	−0.59 (−1.79 to 0.63)	−0.40 (−0.62 to −0.19)
Ethiopia	0.22 (−0.62 to 1.07)	0.10 (−0.85 to 1.06)	0.27 (0.08 to 0.45)
Ghana	0.06 (−0.56 to 0.68)	0.05 (−0.69 to 0.80)	0.06 (−0.08 to 0.20)
Ivory Coast	0.16 (−0.70 to 1.02)	0.08 (−0.90 to 1.08)	0.11 (−0.08 to 0.30)
Kenya	1.21 (0.50 to 1.92)	0.69 (−0.15 to 1.53)	0.72 (0.56 to 0.88)
Lesotho	0.46 (−0.16 to 1.09)	0.52 (−0.15 to 1.19)	0.28 (0.14 to 0.41)
Mozambique	0.98 (0.34 to 1.63)	1.00 (0.27 to 1.74)	0.74 (0.60 to 0.89)
Namibia	2.22 (1.83 to 2.61)	1.99 (1.45 to 2.54)	1.96 (1.85 to 2.07)
Nigeria	1.45 (0.95 to 1.96)	1.48 (0.85 to 2.11)	1.56 (1.44 to 1.67)
Sierra Leone	0.09 (−0.72 to 0.91)	0.08 (−0.85 to 1.01)	0.04 (−0.13 to 0.22)
Sudan	1.88 (1.24 to 2.52)	0.90 (−0.09 to 1.90)	1.09 (0.92 to 1.26)
Uganda	0.44 (−0.28 to 1.17)	0.75 (−0.07 to 1.58)	0.26 (0.11 to 0.41)
Asia			
Afghanistan	0.35 (−0.46 to 1.17)	0.41 (−0.52 to 1.36)	0.27 (0.10 to 0.44)
Armenia	0.01 (−0.49 to 0.52)	0.09 (−0.66 to 0.86)	0.09 (−0.05 to 0.23)
Bangladesh	0.20 (−0.60 to 1.01)	0.06 (−0.99 to 1.11)	0.06 (−0.13 to 0.25)
Bhutan	1.08 (0.29 to 1.87)	0.18 (−0.94 to 1.31)	0.12 (−0.09 to 0.33)
Cambodia	0.46 (−0.35 to 1.28)	0.30 (−0.72 to 1.33)	0.35 (0.16 to 0.53)
India	2.10 (1.40 to 2.81)	1.17 (0.12 to 2.22)	1.40 (1.22 to 1.58)
Jordan	−0.50 (−1.07 to 0.06)	−4.51 (−5.71 to −3.3)	−2.04 (−2.23 to −1.85)
Myanmar	0.11 (−0.56 to 0.78)	0.18 (−0.63 to 1.01)	0.19 (0.04 to 0.33)
Nepal	1.01 (0.34 to 1.68)	0.29 (−0.60 to 1.18)	0.30 (0.14 to 0.46)
Pakistan	0.20 (−0.26 to 0.65)	0.10 (−0.45 to 0.65)	0.26 (0.16 to 0.36)
Philippines	0.51 (−0.09 to 1.11)	0.87 (0.11 to 1.64)	0.99 (0.86 to 1.12)
Sri Lanka	0.95 (0.31 to 1.60)	0.42 (−0.61 to 1.45)	0.44 (0.24 to 0.63)
Tajikistan	0.25 (−0.49 to 1.00)	−0.07 (−1.07 to 0.94)	−1.23 (−1.43 to −1.02)
Timor-Leste	−0.04 (−0.79 to 0.72)	0.12 (−0.80 to 1.04)	0.14 (−0.02 to 0.29)
Viet Nam	0.10 (−0.49 to 0.69)	0.02 (−0.84 to 0.89)	0.02 (−0.13 to 0.18)
South America			
Bolivia	0.23 (−0.45 to 0.92)	−0.01 (−0.92 to 0.91)	−0.01 (−0.18 to 0.16)
Brazil	0.22 (−0.39 to 0.83)	0.07 (−0.90 to 1.06)	0.05 (−0.13 to 0.23)
Colombia	1.47 (0.92 to 2.01)	−0.38 (−1.54 to 0.8)	−0.10 (−0.31 to 0.11)
Peru	0.56 (−0.16to 1.27)	0.26 (−0.82 to 1.36)	0.29 (0.08 to 0.49)
Venezuela	0.07 (−0.48 to 0.61)	0.41 (−0.46 to 1.29)	0.55 (0.39 to 0.70)
North America			
Dominican Republic	0.06 (−0.58 to 0.71)	0.08 (−0.85 to –1.02)	0.07 (−0.10 to 0.24)
El Salvador	0.16 (−0.58 to 0.91)	0.09 (−1.14 to 1.32)	0.06 (−0.16 to 0.28)
Haiti	0.21 (−0.37 to 0.79)	0.03 (−0.68 to 0.75)	0.04 (−0.09 to 0.17)
Honduras	1.07 (0.39 to 1.76)	0.92 (−0.02 to 1.87)	0.76 (0.56 to 0.95)
Oceania			
Kiribati	0.23 (−0.35 to 0.83)	0.01 (−0.68 to 0.67)	−0.02 (−0.14 to 0.11)
Papua New Guinea	0.31 (−0.17 to 0.78)	0.21 (−0.38 to 0.79)	0.21 (0.11 to 0.31)
Europe			
Albania	−0.04 (−0.69 to 0.61)	−0.55 (−1.78 to 0.68)	−0.73 (−0.95 to −0.51)
Belarus	−0.02 (−0.60 to 0.56)	0.07 (−0.92 to 1.08)	0.05 (−0.13 to 0.24)

*EAPC – Estimated annual percentage change; CI – confidence interval; Rates provided in per 100,000 persons.

(GLM) considering gaussian distribution for age standardized rates [17,18]. Further details about EAPC is provided in appendix. Equation (1) provides the mathematical notation of EAPC.

$$ln(ASR_x) = \alpha + \beta x + \varepsilon, \quad (1)$$

where α is the intercept term, β is the slope which correspond to the annual change of $ln(ASR_x)$, x is the calendar year, ε is the error term.

EAPC is calculated as 100 × (exp ($\widehat{\beta}$) - 1), and its 95% confidence interval (CI) is computed similarly from the linear regression model. The deep learning model was created and deployed using Python 3.8

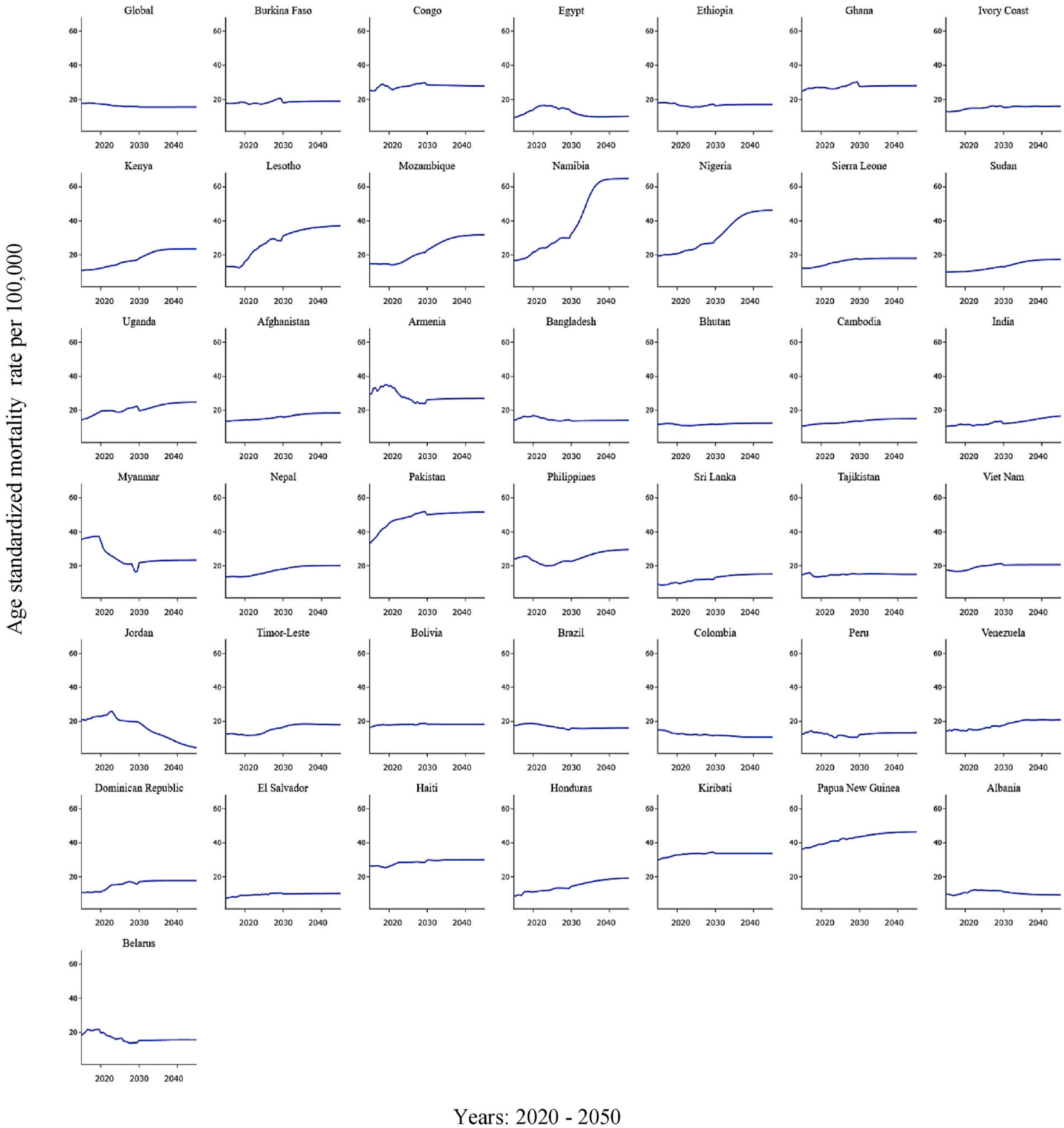


Fig. 2. Projected trend in age standardized breast cancer mortality rate between 2020 and 2050. *Mortality rate been age standardized.

5. Findings

The average age standardized breast cancer incidence, and DALYs rates at global level is expected to remain high with a fractional increase in incidence rate from 45 per 100,000 to 46 per 100,000 population, and fractional increase in DALYs rate from 467 to 477 per 100,000 population between 2020 and 2050, (Figs. 1 and 3, supp. Table 2). However, the global age standardized breast cancer mortality rate is expected to remain constant at 15 per 100,000 population between 2020 and 2050, (Fig. 2, supp. Table 2).

Between 2020 and 2050 most of the countries included in the study are expected to have an increase in exposure risk to high plasma glucose level, high BMI, and SDI between 2020 and 2050. In addition, considerable variation in exposure risk to high plasma glucose

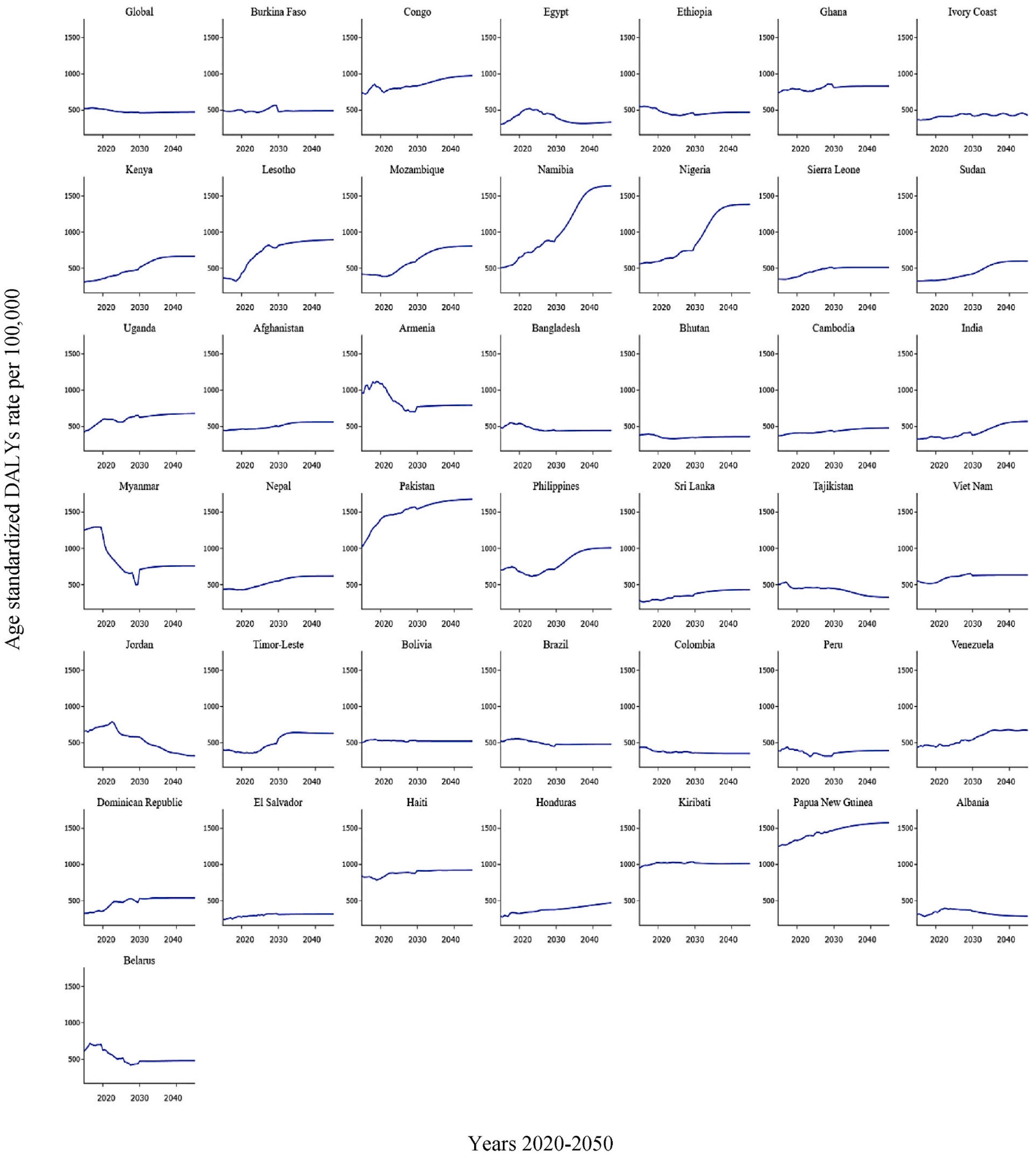
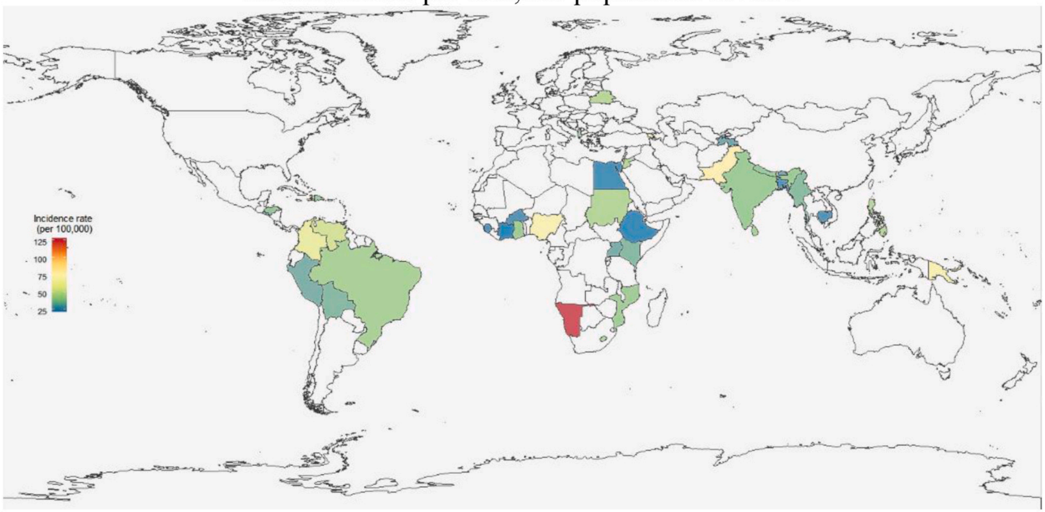
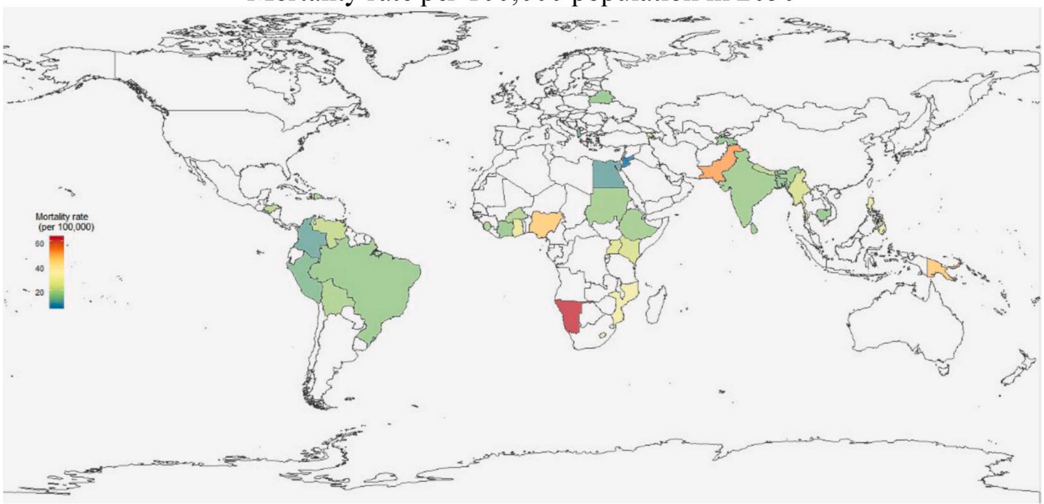


Fig. 3. Projected trend in age standardized breast cancer DALYs rate between 2020 and 2050. *DALYs – disability adjusted life years; DALYs rate has been standardized.

Incidence rate per 100,000 population in 2050



Mortality rate per 100,000 population in 2050



DALYs rate per 100,000 population in 2050

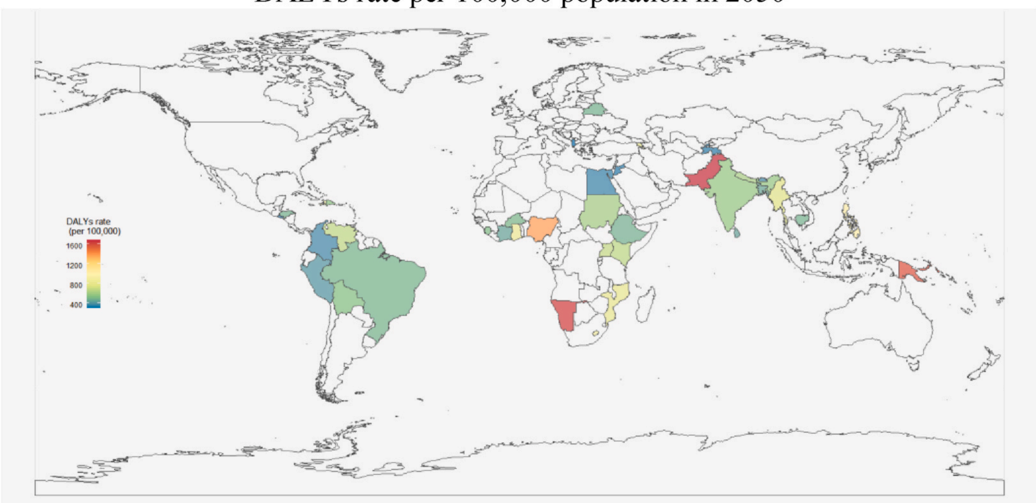


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Fig. 4. Variation in age standardized breast cancer incidence, mortality, and DALYs rates among 42 LMICs in 2050. *DALYs-disability adjusted life years; age standardized rates provided in per 100,000 persons.

level, high BMI, and SDI is observed among 42 LMICs. Predicted result of the risk factors included in the prediction model is provided in appendix, (supp. figures 2–4).

6. Trend in age standardized breast cancer incidence rate (ASIR) in 42 LMICs between 2020 and 2050

6.1. Africa

ASIR is expected to remain high in most of the countries in Africa between 2020 and 2050.13 out of 14 African nations included in the study, are expected to have increase in ASIR between 2020 and 2050. ASIR in 2050 is expected to be highest in Namibia; 127 per 100,000 population, followed by Congo; 74 per 100,000, and Nigeria; 71 per 100,000 in 2050, (Figs. 1 and 4, supp. table 2, supp. figure 5). Estimated annual percentage change (EAPC) in ASIR between 2020 and 2050 is expected to be highest in Namibia 2.22% (95% CI; 1.83–2.61) followed by Sudan, Congo, and Nigeria, respectively. However, Egypt is expected to have declining trend in ASIR between 2020 and 2050 with EAPC -0.16% (95% CI: −0.97 – 0.66), (table 2, supp. figure 8).

6.2. Asia

In Asia, ASIR between 2020 and 2050 is expected to increase in 14 out of 15 countries included in the study. ASIR in 2050 is expected to be highest in Pakistan; 76 per 100,000 population, followed by Armenia, Philippines, and Jordan, (Figs. 1 and 4, supp. table 2, supp. figure 6). EAPC in ASIR between 2020 and 2050 is predicted to be highest in India; 2.10% (95% CI: 1.40–2.81), followed by Bhutan, Nepal, and Sri Lanka, respectively. However, EAPC is expected to have declining trend in Jordan; −0.50% (95%CI: −1.07 – 0.06), (Table 2, supp. figure 8).

6.3. South America, north America, oceania, and europe

Among the South American nations included in the study, ASIR in 2050 is predicted to be highest in Colombia; 61 per 100,000 population, followed by Venezuela, Brazil, Bolivia, and Peru, respectively. EAPC in ASIR between 2020 and 2050 is expected to increase in all the South American countries included in the study with the highest EAPC expected in Colombia; 1.47% (95% CI: 0.92–2.01) followed by Peru, Bolivia, Brazil, and Venezuela, respectively. In North America, ASIR is expected to be highest in Haiti; 47 per 100,000 population, followed by Honduras, Dominican Republic, and El Salvador, respectively. EAPC in ASIR is expected to be positive in all North American countries included in the study with highest EAPC in Honduras; 1.07% (95%CI: 0.39–1.76) followed by Haiti, El Salvador, and Dominican Republic, respectively. Both countries from Oceania region are expected to have an increase in ASIR between 2020 and 2050. ASIR in 2050 in Papua New Guinea is expected to be 71 per 100,000 population; followed by Kiribati. EAPC in Papua New Guinea is expected to be 0.31% (95% CI: −0.17 – 0.78), followed by Kiribati. Both European countries included in the study are expected to have diminutive decline in ASIR between 2020 and 2050. ASIR is expected to decline from 37 per 100,000 to 36 per 100,000 population, in Albania and 47 to 46 per 100, 000 population, in Belarus. EAPC in ASIR is expected to be −0.04% (95% CI: −0.69 – 0.61) in Albania and −0.02% (95%CI: −0.6 – 0.56) in Belarus, (table 2, Figs. 1 and 4, supp. table 2, supp. figures 7&8).

7. Trend in age standardized breast cancer mortality rate (ASMR) in 42 LMICs between 2020 and 2050

7.1. Africa

ASMR is expected to remain high in most of the countries in Africa between 2020 and 2050. Out of 14 African nations included in the study, 12 of them are expected to have increase in the ASMR between 2020 and 2050. ASMR in 2050 is expected to be highest in Namibia; 65 per 100,000 population, followed by Nigeria, Lesotho, and Mozambique, respectively, (Figs. 2 and 4, supp. table 2, supp. figure 9). The highest positive EAPC in ASMR between 2020 and 2050 is expected in Namibia; 1.99% (95% CI: 1.45–2.54), followed by Nigeria, Uganda, and Kenya, respectively. However, Egypt and Congo are expected to have declining EAPC in ASMR between 2020 and 2050, (table 2, supp. figure 12).

7.2. Asia

In Asia, ASMR between 2020 and 2050 is expected to increase in 13 out of 15 countries included in the study. ASMR in 2050 is expected to be highest in Pakistan; 52 per 100,000 population, followed by Philippines, Armenia, and Myanmar, respectively, (Figs. 2 and 4, supp. table 2, supp. figure 10). EAPC in ASMR between 2020 and 2050 is predicted to increase significantly in India; 1.17% (95% CI: 0.12–2.22), followed by Philippines, Sri Lanka, and Afghanistan, respectively. However, ASMR between 2020 and 2050 is expected to have significantly declining trend in Jordan; −4.51% (95% CI: −5.71 to −3.30), (Table 2, supp. figure 12).

7.3. South America, north America, oceania, and europe

Among South American nations included in the study, ASMR in 2050 is predicted to be highest in Venezuela; 21 per 100,000 population, followed by Bolivia, Brazil, Peru, and Colombia. EAPC in ASMR between 2020 and 2050 is expected to be positive in 3 out of 5 South American countries included in the study. The highest EAPC in ASMR between 2020 and 2050 is expected in Venezuela; 0.41% (95% CI: −0.46 – 1.29), followed by Peru, and Brazil. However, Colombia and Bolivia are expected to have declining trend in ASMR between 2020 and 2050 with EAPC of −0.38% (95% CI: −1.54 – 0.80) and −0.01% (95% CI: −0.92 – 0.91), respectively. In North America, all the countries included in the study are predicted to have an increase in ASMR between 2020 and 2050. The highest ASMR in 2050 is expected in Haiti; 30 per 100,000 population, followed by Honduras, Dominican Republic, and El Salvador. EAPC in ASMR between 2020 and 2050 is expected to be highest in Honduras; 0.92% (95% CI: −0.02 – 1.87), followed by El Salvador, Dominican Republic, and Haiti, respectively. In Oceania, Papua New Guinea is expected to have increase in ASMR from 44 per 100,000 population in 2020 to 48 per 100,000 population in 2050. Whereas ASMR is expected to remain constant at 34 per 100,000 population in Kiribati between 2020 and 2050. EAPC in ASMR between 2020 and 2050 is expected to decline in Papua New Guinea; 0.21% (95% CI: −0.38 – 0.79), whereas in Kiribati it is expected to remain constant. In Europe, Belarus is expected to have fractional increase in ASMR from 15 per 100,000 population in 2020 to 16 per 100,000 population with EAPC of 0.07% (95% CI: −0.92 – 1.08). Whereas in Albania, ASMR is expected to decline from 11 per 100,000 to 10 per 100,000 population between 2020 and 2050, (table 2, Figs. 2 and 4, supp. table 2, supp. figures 11&12).

8. Trend in age standardized breast cancer DALYs rate (ASDR) in 42 LMICs between 2020 and 2050

8.1. Africa

ASDR is expected to remain high in most of the countries in Africa between 2020 and 2050.13 out o14 African nations included in the study are expected to have increase in ASDR between 2020 and 2050. ASDR in 2050 is expected to be highest in Namibia; 1638 per 100,000 population, followed by Nigeria, Democratic Republic of Congo, and Lesotho, respectively, (Figs. 3 and 4, supp. table 2, supp. figure 13). The highest EAPC in ASDR between 2020 and 2050 is expected in Namibia; 1.96% (95% CI: 1.85–2.07), followed by Nigeria, Sudan, and Mozambique, respectively. However, Egypt is expected to have declining EAPC in ASDR between 2020 and 2050; −0.40% (95% CI: −0.62 to −0.19), (table 2, supp. figure 16).

8.2. Asia

In Asia, ASDR between 2020 and 2050 is expected to increase in 13 out of 15 countries included in the study. ASDR in 2050 is expected to be highest in Pakistan; 1679 per 100,000 population, followed by Philippines, Armenia, and Myanmar, respectively, (Figs. 3 and 4, supp. table 2, supp. figure 14). The highest increase in EAPC in ASDR between 2020 and 2050 is expected in India; 1.40% (96% CI: 1.22–1.58), followed by Philippines, Sri Lanka, and Cambodia, respectively. However, EAPC in ASDR is expected to have significant decline in Jordan; −2.04% (95% CI: −2.23 to −1.85), and Tajikistan; −1.23% (95% CI: −1.43 to −1.02), (Table 2, supp. figure 16).

8.3. South America, north America, oceania, and europe

Among the South American nations included in the study, ASDR in 2050 is predicted to be highest in Venezuela; 675 per 100,000 population, followed by Bolivia, Brazil, Peru, and Colombia, respectively. EAPC in ASDR between 2020 and 2050 is expected to increase in Venezuela; 0.55% (95% CI: 0.39–0.70), followed by Peru, and Brazil, respectively. However, EAPC in ASDR between 2020 and 2050 is expected to decline in Colombia; −0.10 (95% CI: −0.31 – 0.11) and Bolivia; −0.01% (95% CI: −0.18 – 0.16). In North America, all the countries included in the study are predicted to have an increase in ASDR between 2020 and 2050. The highest ASDR in 2050 is expected in Haiti; 926 per 100,000 population, followed by Dominican Republic, Honduras, and El Salvador, respectively. EAPC in ASDR between 2020 and 2050 is expected to be highest in Honduras; 0.76% (95% CI: 0.56–0.95), followed by Dominican Republic, El Salvador, and Haiti. In Oceania, Papua New Guinea is expected to have increase in ASDR from 1479 per 100,000 population in 2020 to 1581 per 100,000 population in 2050 with EAPC of 0.21% (95% CI: 0.11–0.31). Whereas, in Kiribati, ASDR is expected to have diminutive declining from 1025 per 100,000 population in 2020 to 1018 per 100,000 population in 2050 with declining EAPC of −0.02% (95% CI: −0.14 – 0.11). In Europe, Belarus is expected to have fractional increase in ASDR from 471 per 100,000 in 2020 to 478 per 100,000 population in 2050. EAPC in ASDR between 2020 and 2050 in Belarus is expected to be 0.05% (95% CI: −0.13 – 0.24). However, ASDR in Albania is predicted to decline from 361 per 100,000 in 2020 to 292 per 100,000 population in 2050 with the declining EAPC of −0.73% (95% CI: −0.95 to −0.51), (table 2, Figs. 3 and 4, supp. table 2, supp. figures 15&16).

9. Discussion

Breast cancer is the most commonly diagnosed cancer globally, surpassing the lung cancer [1]. This study provides the comprehensive and independent analysis of breast cancer burden in 42 LMICs between 2020 and 2050. Our study finding suggests age standardized breast cancer incidence, morality, and DALYs rates between 2020 and 2050 will increase in most of the LMICs included in the study with high disparity among countries and regions. ASIR is expected to increase in 38 LMICs in addition to expected increase in ASMR and ASDR in 33 and 35 LMICs out of 42 LMICs between 2020 and 2050. Age standardized breast cancer incidence, mortality, and DALYs rates in 2050 are expected to remain significantly high in Namibia, Pakistan, Nigeria, Papua New Guinea, Lesotho, Kiribati, and Philippines, respectively.

The increasing trend observed in ASIR between 2020 and 2050 in some countries could be due to expected increase in exposure to the breast cancer risk factors such as high plasma glucose level and high BMI in those countries. In addition, the increasing trend could be explained by various other factors such as changes in lifestyles i.e., increase in sedentary lifestyle in conjunction with change in food habits, brought about by growing economies, and urbanization, low physical activity, low fertility rate, and increase in smoking and alcohol consumption, [19,20]. All the above-mentioned risk factors and causes could also explain the predicted increase in ASMR and ASDR. Furthermore, low breast cancer survival rate in LMICs could also be an important reason for the expected increase in ASMR in the future.

Reasons for low survival rate in LMICs are complex involving individual, interpersonal, organizational, community, and policy issues [21,22]. Firstly, absence of early detection programs in LMICs implies that significant number of cases with breast cancer are presented at an advanced stage (i.e., clinical stage III or IV) resulting in worse outcomes such as treatment complication and low survival rate increasing the risk of death [22–24]. Secondly, even when breast cancers are detected early, treatment choices are often limited, or otherwise less accessible in comparison to HICs [25]. Third, breast cancer is not recognized as a priority in many LMICs due to the load of communicable disease burden, lack of funding, lack of political commitment, and lack of skilled human resources in health sector [26,27]. Therefore, given the burden of breast cancer in LMICs, there is a pressing need to explore strategies by which the survival rates as well as the quality of life could be improved [28,29]. There is a notable delay between symptom onset and seeking healthcare in LMICs leading to high breast cancer burden [22,30]. Thus, to reduce the burden of breast cancer in LMICs, early detection of breast tumors through breast self-examination (BSE), clinical breast examination (CBE), and clinical downstaging recommended by the Breast Health Global Initiative (BHGI) should be effectively implemented [30,31]. Governments, policy makers and the stakeholders should focus on formulating tailored strategies and ensure effective implementation of these strategies and initiatives through evidence-based practices. However, it is important to note that improved in breast cancer diagnosis services in LMICs would likely lead to an increase in reported breast cancer incidence due to stage shifting. However, without improved multimodality treatment, this may not result in a substantial reduction in breast cancer mortality and DALYs [32].

In addition, our study finding shows considerable variation in estimated age standardized breast cancer incidence, mortality, and DALYs rates across the region. For instance, the variation in estimated ASIR in 2050 range from 21 per 100,000 population in Ivory Coast to 127 per 100,000 population in Nigeria. Such remarkable geographical contrasts reflect differences in exposure to risk factors and serious inequalities in access to adequate screening and effective treatment facilities [33,34].

A few countries such as Egypt, Jordan, Albania, Belarus are expected to have decline in age standardized breast cancer incidence, rate. Furthermore, countries such as Tajikistan, Kiribati, Bolivia, and Colombia are expected to have decline in ASMR and ASDR between 2020 and 2050. This could be due to persisting declining trend in breast cancer incidence, mortality, and DALYs rates in recent years and expected decrease in exposure risk to high plasma glucose level and high BMI in these countries between 2020 and 2050. In contrast, the forecasted results presented by GLOBOCAN study shows increasing trend in ASIR and ASMR between 2020 and 2040 in these countries [35,36]. This could be due to difference in forecasting model used by GLOBOCAN study. IARC employed Power 5 and Poisson Age-Period-Cohort (APC) models to predict cancer incidence and mortality estimates [36]. This model is based on spatial correlation of age, period, and cohort and do not incorporate any predictors [37]. APC model is the general model which is not specific to the risk factors and socio-demographic indicators in particular region or country [37]. However, the RNN-LSTM model used in our study is a semi-supervised learning model where the model outputs are solely based on the behavior of past data and its attributes i.e., predictors included (high fasting plasma glucose, high BMI, and SDI). Thus, the forecasted estimates yielded by GLOBOCAN study differ compared to the findings of our study.

10. Strengths and limitations

This study provides future estimates and trends in age-standardized breast cancer incidence, mortality, and DALYs rates in 42 LMICs between 2020 and 2050. The RNN-LSTM prediction model resolves the issues of non-stationarity, assumption of normal distribution, and co-integration in timeseries data hence providing reliable and robust estimates. Our study has several limitations. Breast cancer screening services availability and accessibility is a prominent factor in determining breast cancer related burden. However, due to insufficient data these factors were not included in the prediction model which could have yielded a more robust outcome. In addition, breast cancer incidence, mortality, and DALYs rates vary among different socio-economic groups and regions within a country. However, subnational analysis could not be performed to analyze subnational disparity due to limited data availability. Lastly, change in population size and demographic structure of the population over time were not considered in the model. Thus, including these factors could have led to different prediction estimates.

11. Conclusion

In conclusion, this study provides a comprehensive descriptive epidemiology of breast cancer and its heterogeneity in 42 LMICs around the globe. It provides the clear projected trajectory of breast cancer burden in 42 LMICs between 2020 and 2050. The burden of breast cancer is expected to increase in most of the LMICs between 2020 and 2050 with prominent regional disparity. This study could serve as a useful reference to monitor the progress towards achieving the target of GBCI to reduce global breast cancer mortality by

2.5% per year by 2040. To reduce the increasing burden of breast cancer in LMICs, focus should be on minimizing the exposure to the modifiable risk factors such as high fasting plasma glucose, and high BMI. In addition, formulating tailored strategies to raise awareness about breast cancer and its related risk factors could help in monitoring the rising burden of breast cancer in LMICs.

Ethics approval

Ethical approval was not required for this secondary analysis of publicly available data.

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Authorship contributions

Santosh Kumar Rauniyar, Daisuke Yoneoka, Masahiro Hashizume, and Shuhei Nomura – Conceived and designed the research study.

Santosh Kumar Rauniyar, Masahiro Hashizume, and Shuhei Nomura; acquired and curated the data.

Santosh Kumar Rauniyar, Daisuke Yoneoka, and Shuhei Nomura; analyzed and interpreted the data:

Santosh Kumar Rauniyar, Daisuke Yoneoka, Masahiro Hashizume, and Shuhei Nomura; interpreted and analyzed the findings. t.

Santosh Kumar Rauniyar, Daisuke Yoneoka, Masahiro Hashizume, and Shuhei Nomura; wrote and revised the paper.

Data availability statement

Data associated with this study has been deposited at https://vizhub.healthdata.org/gbd-results.

Article summary

What is already known to the topic

- The global burden of breast cancer increasing trend, and it has surpassed lung cancer as the most prevalent cancer in world.
- Significant variation in burden of breast cancer is observed between the high-income countries (HICs) and the low-and middle-income countries.

What this study adds

- This study provides future estimates for breast cancer burden in 42 LMICs along with the estimates of risk factors such as high plasma glucose level, high BMI and SDI between 2020 and 2050.
- Age standardized breast cancer incidence, mortality, and DALYs rates between 2020 and 2050 are expected to increase in most of the LMICs with significant variation across the regions.

How this study might affect research, practice, and/or policy

- The finding of our study could assist in further strengthening the strategies and action-plan to prevent and manage breast cancer burden in LMICs.
- It could serve as a useful reference to monitor the local progress towards achieving the target of Global Breast Cancer Initiative (GBCI) to reduce global breast cancer mortality by 2.5% per year by 2040.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e16427.

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