



# GLOBAL BURDEN OF FEMALE CANCERS ATTRIBUTABLE TO HIGH BODY MASS INDEX, 1990–2021: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2021

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## INTRODUCTION

Obesity has emerged as a critical global health challenge and is now recognized as a major metabolic risk factor for cancer. According to GBD 2019, high BMI contributed to more than 460,000 cancer deaths and 11 million DALYs, ranking as the third leading cancer risk factor in females after tobacco and unsafe sex (Zhi et al., 2022; GBD 2019 Cancer Risk Factors Collaborators, 2022). The impact is particularly pronounced in female-specific cancers such as breast, uterine, and ovarian cancers, where adiposity-driven hormonal, inflammatory, and metabolic mechanisms amplify risk (Iyengar et al., 2016; Lauby-Secretan et al., 2016). However, most global assessments rely on GBD 2019 estimates, overlooking updated GBD 2021 data that capture the period up to 2021, including potential impacts of the COVID-19 pandemic. Furthermore, while socio-demographic, age, and geographic patterns have been examined for general cancer burden in previous GBD studies, these dimensions remain underexplored in the context of female-specific cancers and obesity, limiting the development of targeted prevention strategies.

## OBJECTIVES

- Provide an updated analysis of female cancers attributable to high BMI using GBD 2021.
- Quantify and compare burden across breast, uterine, ovarian, and cervical cancers.
- Assess temporal trends (1990–2021) and identify SDI-level and age-specific patterns.
- Map geographic variation and highlight emerging regional hotspots.
- Project incidence and prevalence to 2030 using ARIMA modeling.
- Inform sex- and region-specific prevention strategies targeting obesity as a modifiable risk factor.

## METHODOLOGY



- **Data source:** Global Burden of Disease (GBD) 2021 (IHME)
- **Primary metrics:** Disability-adjusted life years (DALYs) and age-standardized DALY rates (ASDRs).
  - DALYs combine premature mortality (YLLs) + disability (YLDs), enabling cross-country and cross-cancer comparisons.
  - ASDRs adjust for population age structure, ensuring comparability across time and regions.
- **R-Based Analyses:**
  - Risk-attributable burden by cancer type.
  - Temporal trends (1990–2021).
  - SDI-level and age-specific patterns.
  - Geographic heatmaps (sex-specific & pooled quintiles).
  - Projections to 2030 with ARIMA models (validated by AIC, MAPE <3%, Ljung-Box test).

## RESULTS & DISCUSSION

### GLOBAL FEMALE CANCER BURDEN 2021

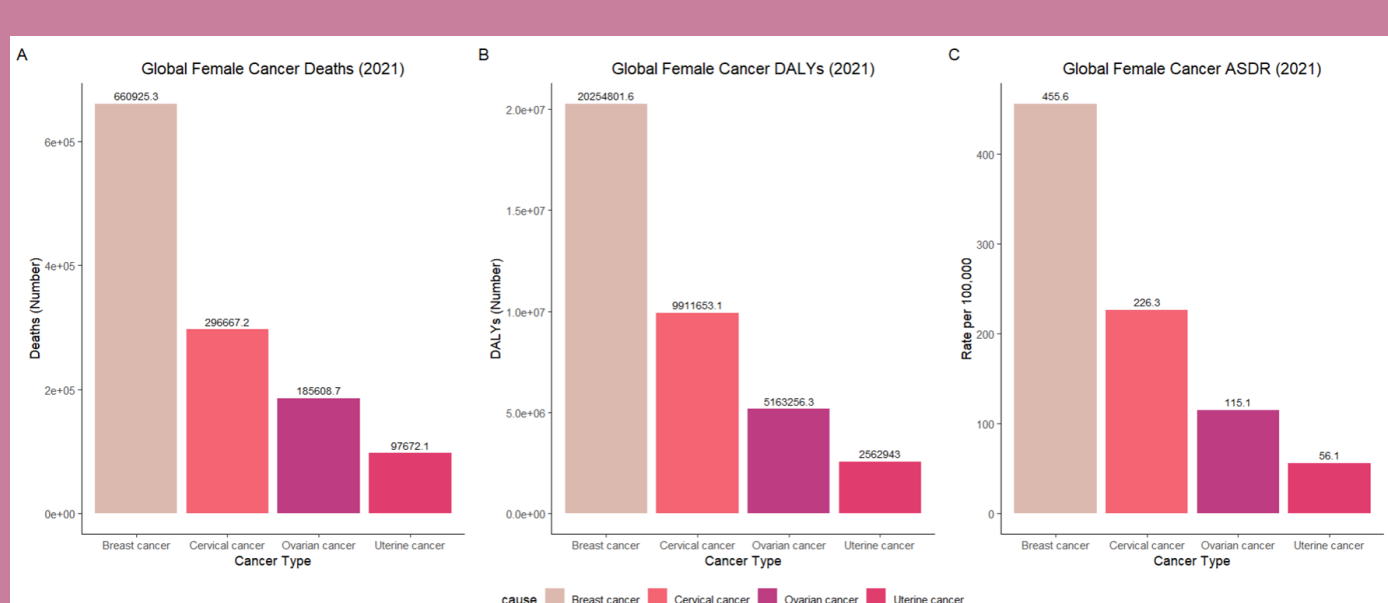


Figure 1: Global Burden of Female Cancers in 2021. (a) Crude death counts; (b) Crude DALY counts; (c) Age-standardized DALY rates

- **Burden hierarchy:** Breast cancer leads (661k deaths; 20.3M DALYs), followed by cervical (297k; 9.9M), ovarian (186k; 5.2M), and uterine (98k; 2.6M).
- **ASDRs:** Breast cancer highest (456/100k), then cervical (226), ovarian (115), uterine (56).
- **Comparative context:** Patterns align with GBD 2019 estimates (GBD 2019 CRF, 2022; GBD 2019 D&I, 2020), reaffirming breast cancer as the leading global female cancer burden.
- **Significance:** Cervical cancer's high rate reflects persistent need for prevention in LMICs, while breast cancer sets the baseline for examining BMI-related contributions in later sections.

### HBMI AS A MAJOR RISK FACTOR AND 1990-2021 TREND

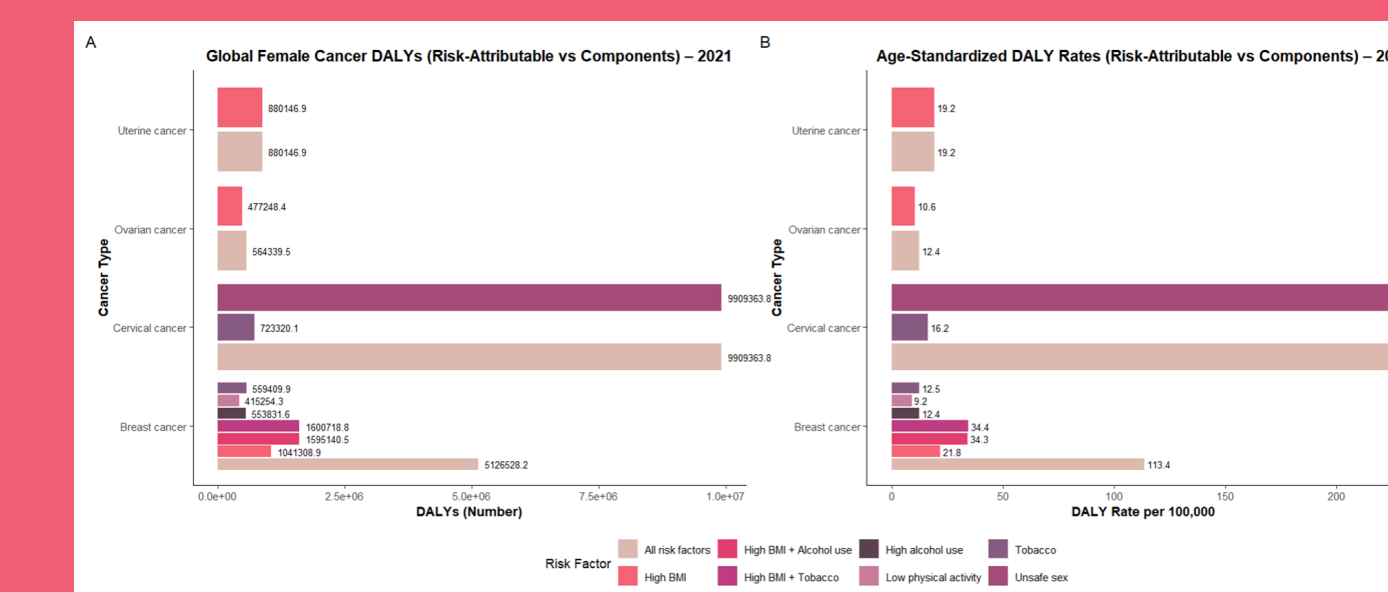


Figure 2 (a-b). Comparison of Specific Risk Attributable vs. Total Risk attributable Disease Burden for Female Cancers in 2021. (a) Crude DALY counts; (b) Age-standardized DALY rates

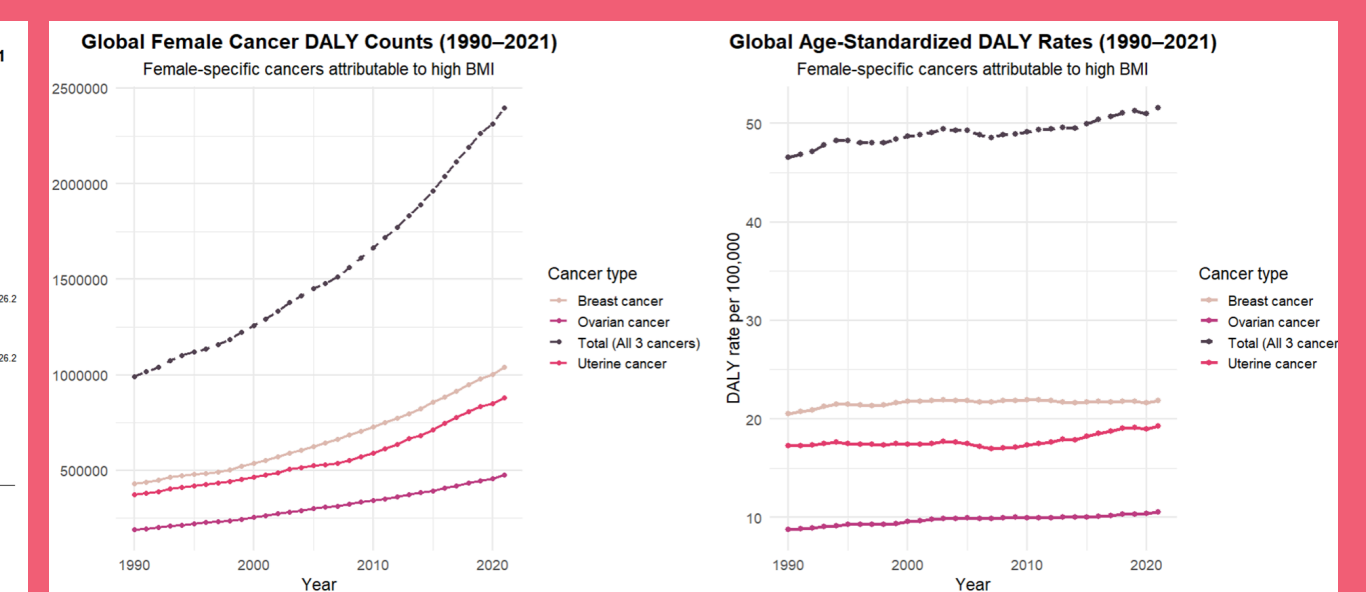


Figure 3 (a-b). Temporal Trends for Female Tumor Disease Burden Attributable to High-BMI as Risk Factor from 1990-2021. (a) Crude DALY counts; (b) Age-standardized DALY rates

### Results & Discussion:

- **High BMI:** Ranks third global cancer risk after tobacco & unsafe sex (GBD 2019 CRF, 2022).
- **Uterine cancer:** Sole risk modeled; BMI = 100% of risk-attributable DALYs (~880k), ~35% of total DALYs (2.6M). Obesity is a major causal factor, with risks up to 7-fold higher in obese women (Lauby-Secretan et al., 2016).
- **Ovarian cancer:** BMI = 477k (~85% of risk-attributable DALYs, 564k), ~9% of total DALYs (5.2M).
- **Breast cancer:** >1M DALYs from BMI (~20% of risk-attributable DALYs, 5M), ~5% of total DALYs (20.3M) → reflects multifactorial etiology.
- **Cervical cancer:** Entirely unsafe sex/HPV; risk-attributable = total DALYs (9.9M).
- **Trends (1990-2021):** DALY counts >doubled, but ASDRs stable → growth driven by population ageing (GBD 2019 D&I, 2020).
- **Implication:** Obesity prevention offers highest yield for uterine & ovarian cancers, while breast cancer requires broader multi-risk strategies.

### SDI Level Trends and Age Specific Burden (2021)

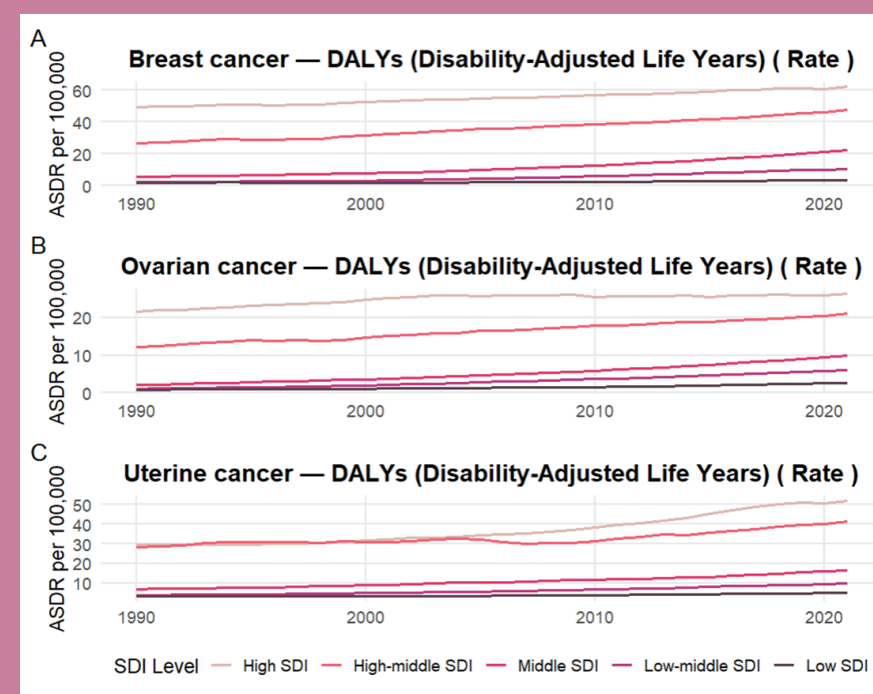


Figure 4 (a-c). Temporal Trends in High BMI-Attributable Burden of Female Cancers by SDI Level From 1990-2021. (a) Breast Cancer ASDR (b) Ovarian Cancer ASDR and (c) Uterine Cancer ASDR

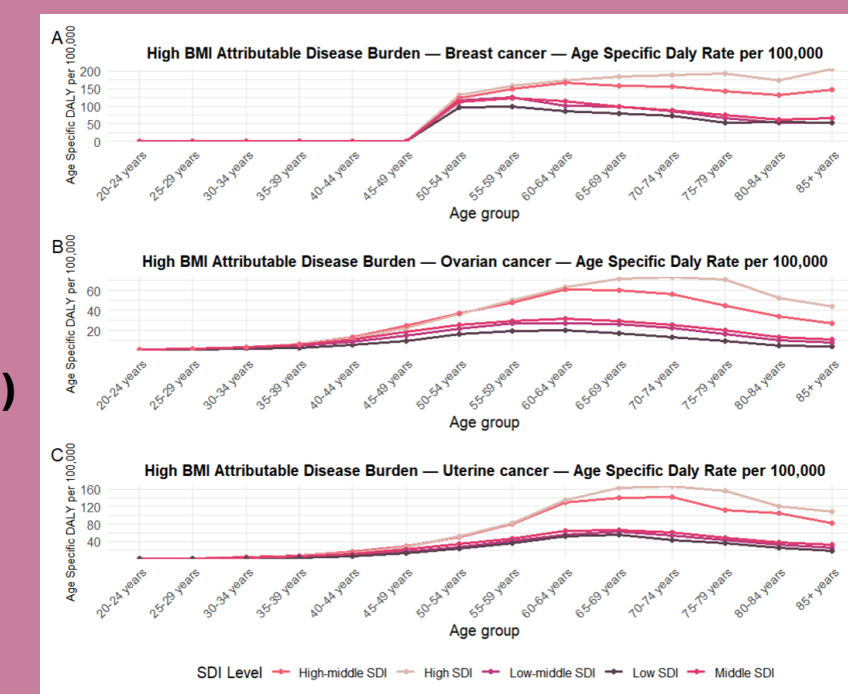


Figure 5. Age Specific Disease Burden for Each Cancer Type in 2021 in Different SDI Levels. (a) Breast Cancer Age-Specific DALY Rates and (b) Ovarian Cancer Age-Specific DALY Rates and (c) Uterine Cancer Age-Specific DALY Rates

### Results & Discussion:

- **High-middle SDI:** Steepest post-2010 increases, mirroring global spread of obesogenic lifestyles (NCD-RisC, 2021; GBD 2019 Cancer Risk Factors Collaborators, 2022).
- **High SDI:** Highest absolute burdens but slower growth, reflecting earlier obesity plateau.
- **Post-menopausal peak:** Driven by adipose-derived estrogen, inflammation, insulin resistance (Iyengar et al., 2016).
- **Relevance:** After menopause, adipose tissue becomes the main source of estrogen, making obesity a particularly strong driver of hormone-sensitive cancers.
- **Uterine cancer:** Strongest causal obesity link, consistent with IARC findings (Lauby-Secretan et al., 2016).
- **Breast cancer plateau >70y:** May reflect competing mortality risks in older ages.
- **Implication:** Prioritize age-targeted (post-menopausal) and region-specific (high-/high-middle SDI) prevention.

### Geographical and Temporal Analysis

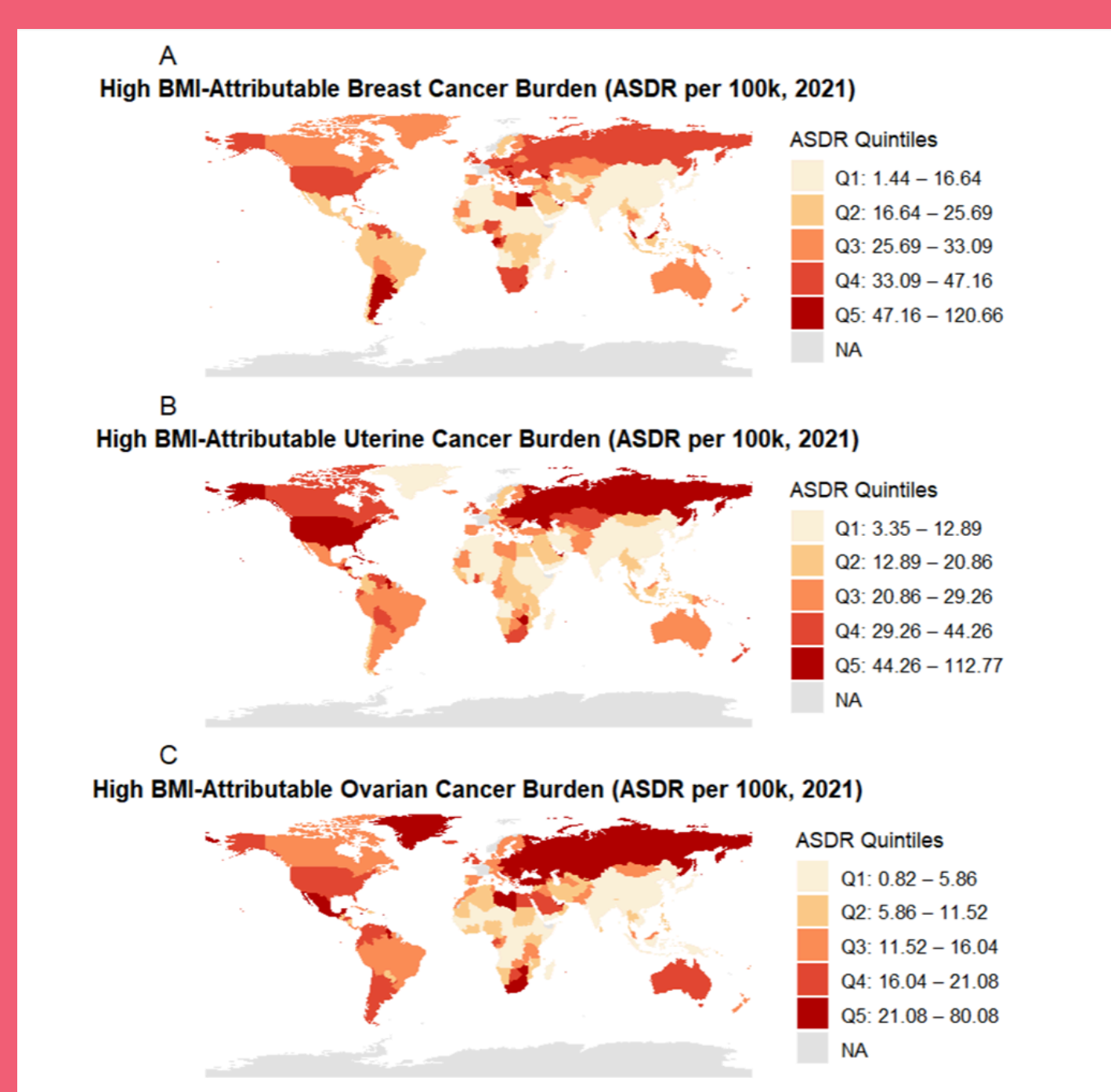


Figure 6: Individual Heatmaps for Each Female Tumour (2021) (a) Breast Cancer, (b) Uterine Cancer, (c) Ovarian Cancer

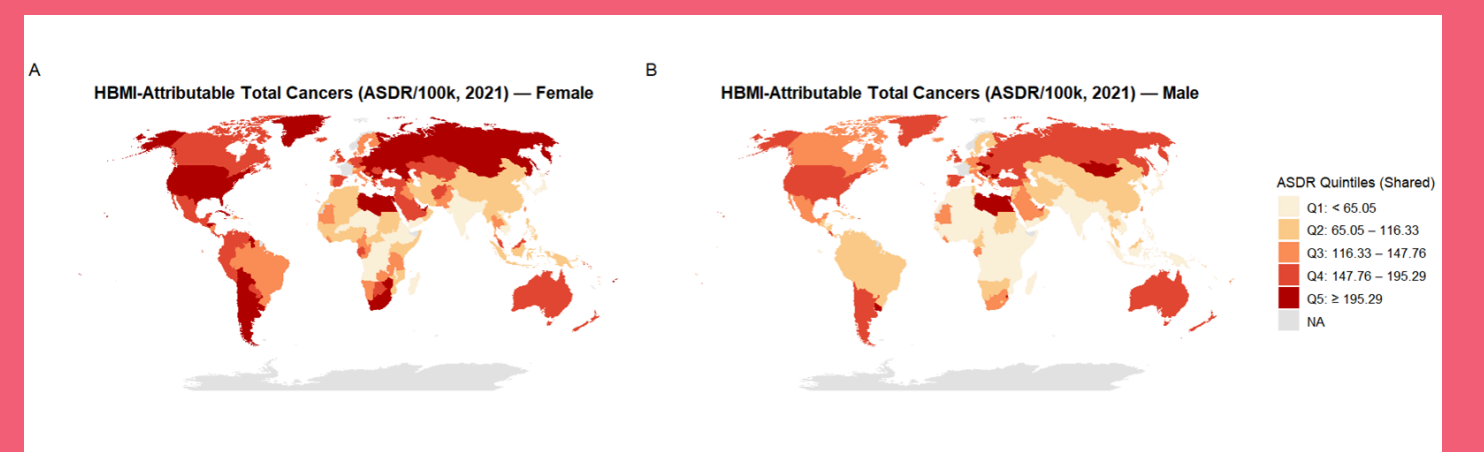


Figure 7. High BMI-Attributable Total Cancer Burden (ASDR/100k, 2021) - by Sex (Pooled Quintiles)

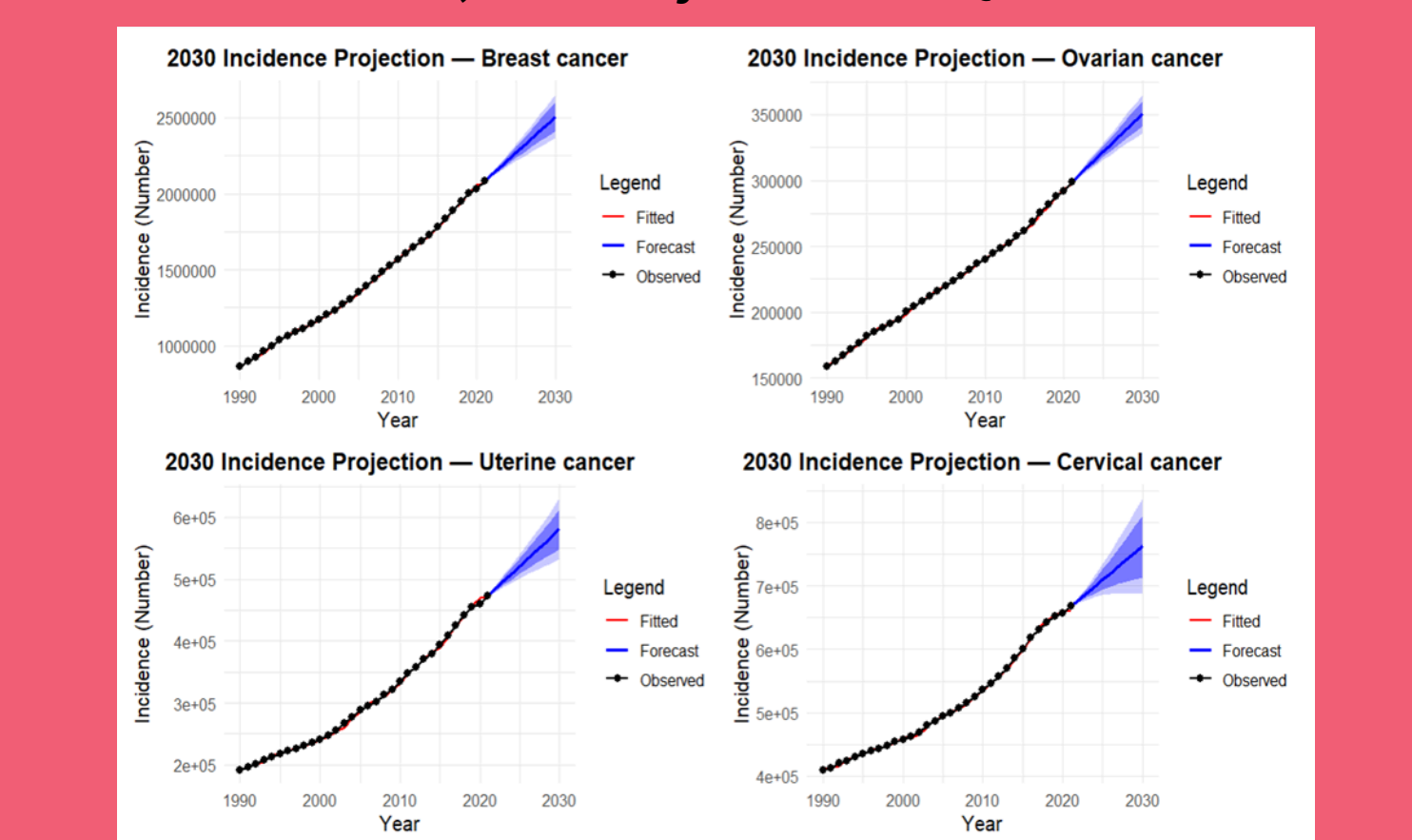


Figure 8: Individual Heatmaps for Each Female Tumour (2021) (a) Breast Cancer, (b) Uterine Cancer, (c) Ovarian Cancer, (d) Cervical Cancer

### Results & Discussion

- **Regional heterogeneity:** High-SDI = largest absolute burden; high-middle SDI = fastest growth (Afshin et al., 2017; GBD 2019 CRF, 2022).
- **Emerging hotspots:** Central Asia, Middle East, and Argentina show notably high BMI-attributable burdens.
- **Mechanistic plausibility:** Elevated uterine & ovarian burdens in hotspot regions align with estrogen, inflammation, insulin/IGF pathways (Iyengar et al., 2016; Lauby-Secretan et al., 2016).
- **Relevance:** These cancers are hormone-sensitive; after menopause, adipose tissue becomes the dominant estrogen source, and obesity-driven metabolic dysfunction amplifies tumor growth.
- **Counts vs rates:** Rising DALY counts but stable ASDRs highlight demography as main driver (GBD 2019 D&I, 2020).
- **Forward risk:** Rising BMI prevalence globally supports continued cancer growth, consistent with 2030 ARIMA forecasts (NCD-RisC, 2021).
- **Projections:** Breast cancer projected to exceed 2.5M new cases annually by 2030, with growth also in ovarian and uterine cancers.
- **Policy:** Strengthen obesity prevention in high-/high-middle SDI and maintain comprehensive risk control in high-SDI settings.

## SUMMARY & FUTURE STEPS

### Summary:

This study provides an updated analysis of female cancers attributable to high BMI using GBD 2021 data, extending beyond prior GBD 2019 estimates. In 2021, high BMI contributed more than 1.9 million DALYs, with breast cancer accounting for the largest absolute burden (~1 million DALYs), uterine cancer showing the highest proportional dependence (~35%), and ovarian cancer also demonstrating substantial attribution (~9%). Since 1990, the burden has more than doubled, with the most rapid increases observed in high-middle SDI regions. Geographic hotspots were identified in North America, Europe, Central Asia, and Southern Latin America, while ARIMA projections indicate continued growth, with breast cancer incidence expected to surpass 2.5 million new cases annually by 2030.

### Future steps:

- Develop obese cancer mouse models (diet-induced, ovariectomized) to study mechanisms.
- Perform RNA-seq and immunologic profiling of tumor and adipose samples.
- Identify hormonal, inflammatory, and metabolic pathways linking obesity to uterine and ovarian cancers.
- Translate findings into prevention and intervention strategies.

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