

# Triple-Negative Breast Cancer on the Rise: Breakthroughs and Beyond [Response to Letter]

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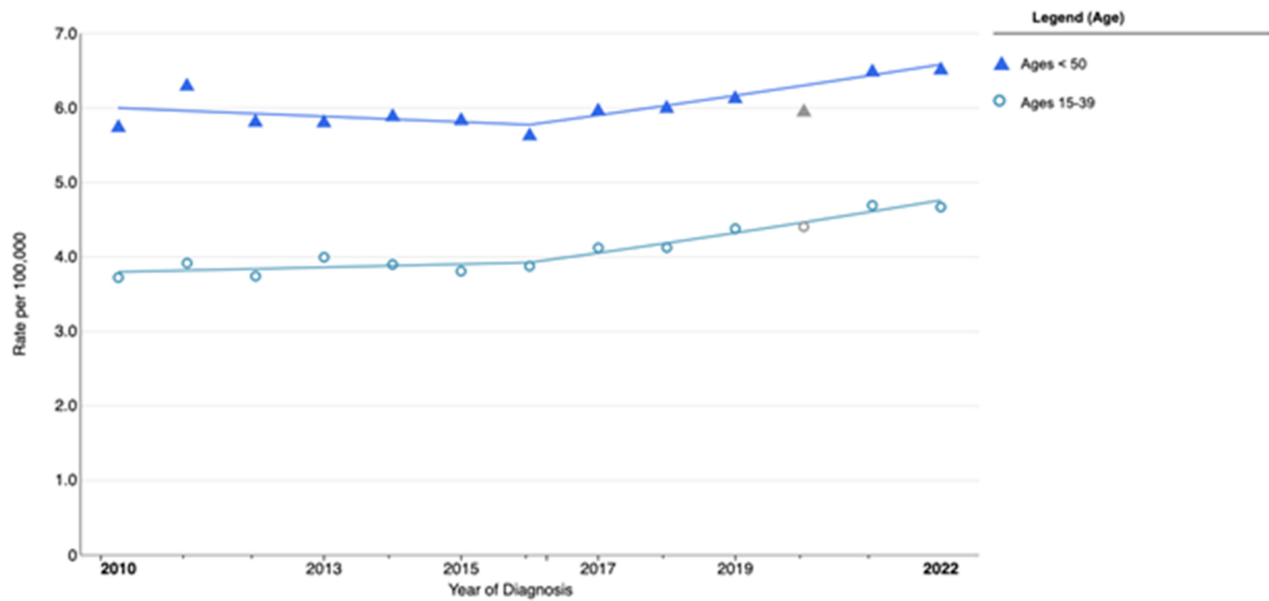
## Dear editor

We appreciate the thoughtful commentary provided by Drs. Lonning, Nikolaienko and Knappskog in response to our article published in June 2025.

The correspondents bring forth several interesting points regarding molecular characterization of hormone receptor-positive (HR+) and hormone receptor-negative (HR-) breast cancers. In our view, these statements and the associated references in their letter (refs. 8–19) do not specifically address the question of TNBC epidemiology among younger patients and are beyond the scope of our article. It should be noted that several of the references cited are authored by the correspondents and while these studies aim to better define the molecular pathogenesis of breast cancer subtypes, they are beyond the scope of this work and the disputed claim.

To address and clarify the concern brought forth by Drs. Lonning, Nikolaienko and Knappskog, we independently consulted the most recently available information from the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) database, which is a trusted resource for detailed statistics about various cancers and subgroupings by age, gender, ethnicity and histology.<sup>1</sup> These results summarized below show a statistically significant increase in incidence of TNBC during the years 2016–2022 among women in age groups 15–39 and below 50 (Figure 1). Likewise, the increased incidence of TNBC during this time period is apparent among women aged 50–64 and above 65 (Figure 2). Finally, while HR+/HER2- breast cancers account for the majority of the increased incidence in total breast cancer cases among females below age 50, as previously reported, recent data show a significant increase in TNBC incidence in this younger group (Figure 3).

**HR-/HER2- Breast Cancer (Female only)**  
**Recent Trends in SEER Age-Adjusted Incidence Rates, 2010-2022**  
**Female By Age, Delay-adjusted SEER Incidence Rate, All Races / Ethnicities, All Stages**



**Data Source:**  
 • SEER Incidence Data, November 2024 Submission (1975-2022). SEER 21 registries [https://seer.cancer.gov/registries/terms.html].

**Methodology:**  
 • Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (20 age groups - Census P25-1130).  
 • The Annual Percent Change (APC) and Average Annual Percent Change (AAPC) estimates were calculated from the underlying rates using the Joinpoint Trend Analysis Software [https://surveillance.cancer.gov/joinpoint]. Version 5.4, April 2023, National Cancer Institute using the default settings.  
 • The APC/AAPC's direction is "Rising" (↑) when the entire 95% confidence interval (C.I.) is above 0, "Falling" (↓) when the entire 95% C.I. is lower than 0, otherwise, the trend is considered "Not Significant".  
 • The 2020 incidence rate(s) were not used in the fit of the trend line(s) and are displayed on the graph as gray data points. Impact of COVID on SEER Cancer Incidence 2020 data [https://seer.cancer.gov/data/covid-impact.html].

**Race/Ethnicity Coding:**  
 • For more details on SEER race/ethnicity groupings, please see Race and Hispanic Ethnicity Changes [https://seer.cancer.gov/seerstat/variables/seertrace\_ethnicity].  
 • Rates for American Indians/Alaska Natives only include cases that are in a Purchased/Referred Care Delivery Area (PRCOA).  
 • Incidence data for Hispanics and Non-Hispanics are based on the NACCR Hispanic/Latino Identification Algorithm (NHIA).

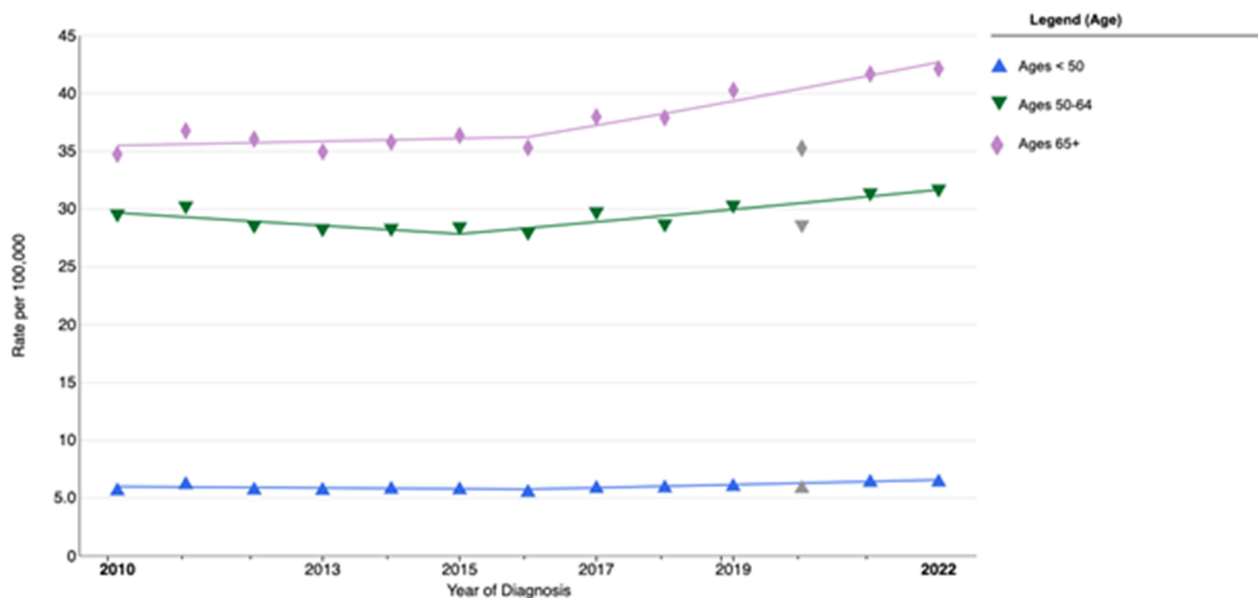
**Cancer Site Coding:**  
 • See SEER Explorer Cancer Site Definitions [https://seer.cancer.gov/statistics-network/explorer/cancer-sites.html] for details about the cancer site coding used for SEER Incidence data.  
 • Stage at diagnosis is calculated using the Combined Summary Stage (2004+) recode, created from SEER Combined Summary Stage 2000 (2004-2017) & Derived Summary Stage 2018 (2018+). For more information, see the SEER documentation [https://seer.cancer.gov/seerstat/variables/seertrd-stage].  
 Created by https://seer.cancer.gov/statistics-network/explorer/ on Wed Sep 03 2025.

**Regression Line Segment Trends (shown on graph)**

Age	Annual Percent Change (APC) Estimates					
	Year Range	APC (%)	Lower 95% C.I.	Upper 95% C.I.	P-Value	Direction
Ages < 50	2010-2016	-0.6	-4.0	0.4	0.23	Not Significant
	2016-2022	2.2	1.0	4.9	<0.01	↑
Ages 15-39	2010-2016	0.5	-4.1	4.7	0.74	Not Significant
	2016-2022	3.3	1.6	6.6	0.01	↑

Figure 1 SEER 21 delay-adjusted incidence rates of HR-/HER2- breast cancer among females aged 15–39 and <50.

**HR-/HER2- Breast Cancer (Female only)**  
**Recent Trends in SEER Age-Adjusted Incidence Rates, 2010-2022**  
**Female By Age, Delay-adjusted SEER Incidence Rate, All Races / Ethnicities, All Stages**



**Data Source:**  
 • SEER Incidence Data, November 2024 Submission (1975-2022). SEER 21 registries [https://seer.cancer.gov/registries/terms.html].

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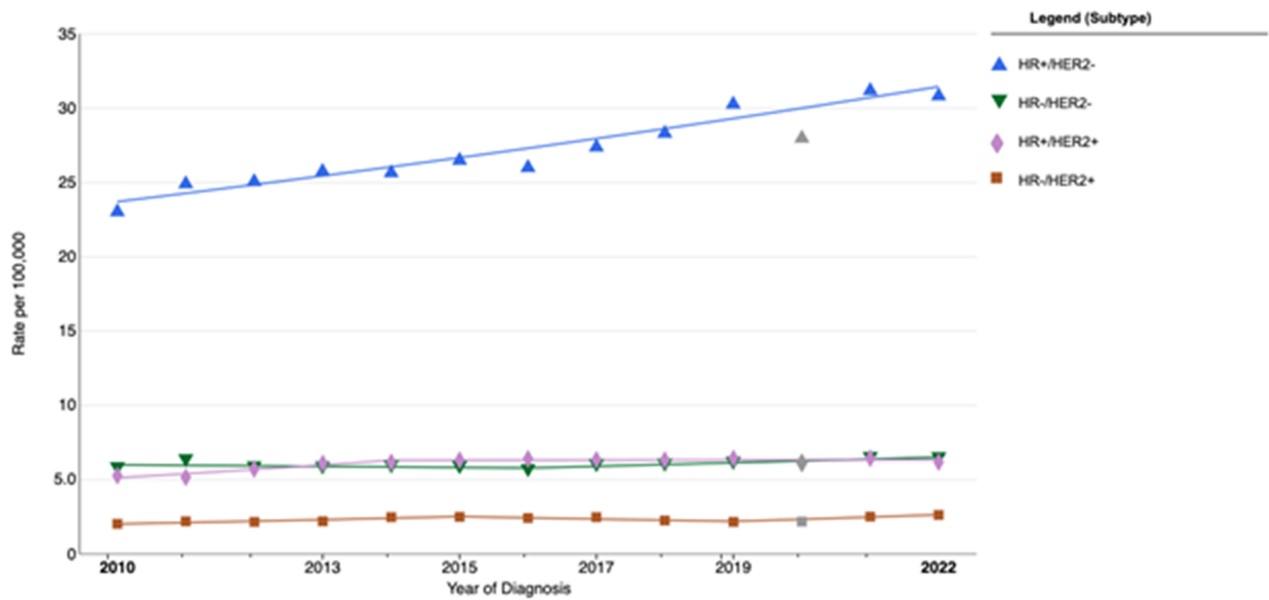
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	Year Range	APC (%)	Lower 95% C.I.	Upper 95% C.I.	P-Value	Direction
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	2016-2022	2.2	1.0	4.9	<0.01	↑
Ages 50-64	2010-2015	-1.3	-5.0	0.2	0.09	Not Significant
	2015-2022	1.9	0.9	4.3	<0.01	↑
Ages 65+	2010-2016	0.3	-3.7	2.0	0.85	Not Significant
	2016-2022	2.8	1.4	5.6	<0.01	↑

Figure 2 SEER 21 delay-adjusted incidence rates of HR-/HER2- breast cancer among females aged <50, 50–64 and 65+.

**Breast**  
**Recent Trends in SEER Age-Adjusted Incidence Rates, 2010-2022**  
**Observed SEER Incidence Rate By Subtype, Female, All Races / Ethnicities, Ages < 50, All Stages**



**Data Source:**  
 • SEER Incidence Data, November 2024 Submission (1975-2022). SEER 21 registries [https://seer.cancer.gov/registries/terms.html]

**Methodology:**  
 • Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (20 age groups - Census P25-1130).  
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 Created by https://seer.cancer.gov/statistics-network/explorer/ on Wed Sep 03 2025.

**Regression Line Segment Trends (shown on graph)**

Subtype	Annual Percent Change (APC) Estimates					
	Year Range	APC (%)	Lower 95% C.I.	Upper 95% C.I.	P-Value	Direction
HR+/HER2-	2010-2022	2.4	1.8	3.0	<0.01	↑
HR-/HER2-	2010-2016	-0.6	-3.9	0.4	0.23	Not Significant
	2016-2022	2.0	0.9	4.6	<0.01	↑
HR+/HER2+	2010-2014	5.3	3.5	8.2	<0.01	↑
	2014-2022	0.1	-0.8	0.7	0.93	Not Significant
HR-/HER2+	2010-2015	4.5	2.8	7.6	<0.01	↑
	2015-2019	-3.4	-7.0	-1.2	<0.01	↓
	2019-2022	6.3	2.8	9.7	<0.01	↑

Figure 3 SEER 21 observed incidence rate by breast cancer subtype in females below age 50. (Delay-adjusted rate currently unavailable for this grouping on SEER database).

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## Disclosure

The authors report no conflicts of interest in this communication.

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## Reference

1. SEER\*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance research program, National Cancer Institute; 2025. Data source(s): SEER Incidence Data, November 2024 Submission (1975-2022), SEER 21 registries.[cited September 3, 2025]. Available from: <https://seer.cancer.gov/statistics-network/explorer/>. Accessed September 16, 2025.

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