

Does Long-Term Exposure to Opioid Lead to Higher Risk of Breast Cancer Recurrence? An Observational Study Using U.S. Population Data

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Background

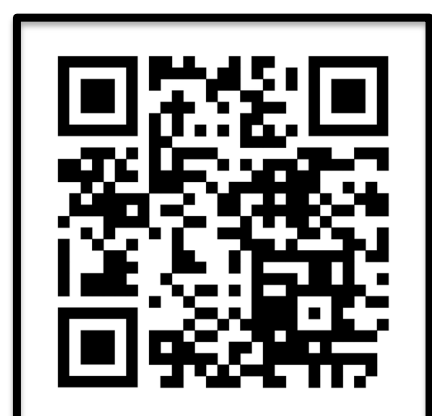
- As cancer survival rates improve, the U.S. cancer survivor population is projected to reach 26 million by 2040.¹
- Chronic pain affects 20–50% of cancer survivors and is commonly managed with opioids during treatment, yet 15–38% of survivors continue opioid therapy into disease-free survivorship.²⁻⁷
- Evidence on persistent opioid use and its health consequences in disease-free survivors remains limited, while emerging preclinical and clinical data suggest opioids may promote tumor growth.⁸

Objectives

- To evaluate the association between long-term opioid exposure and cancer recurrence in disease-free breast cancer survivors.

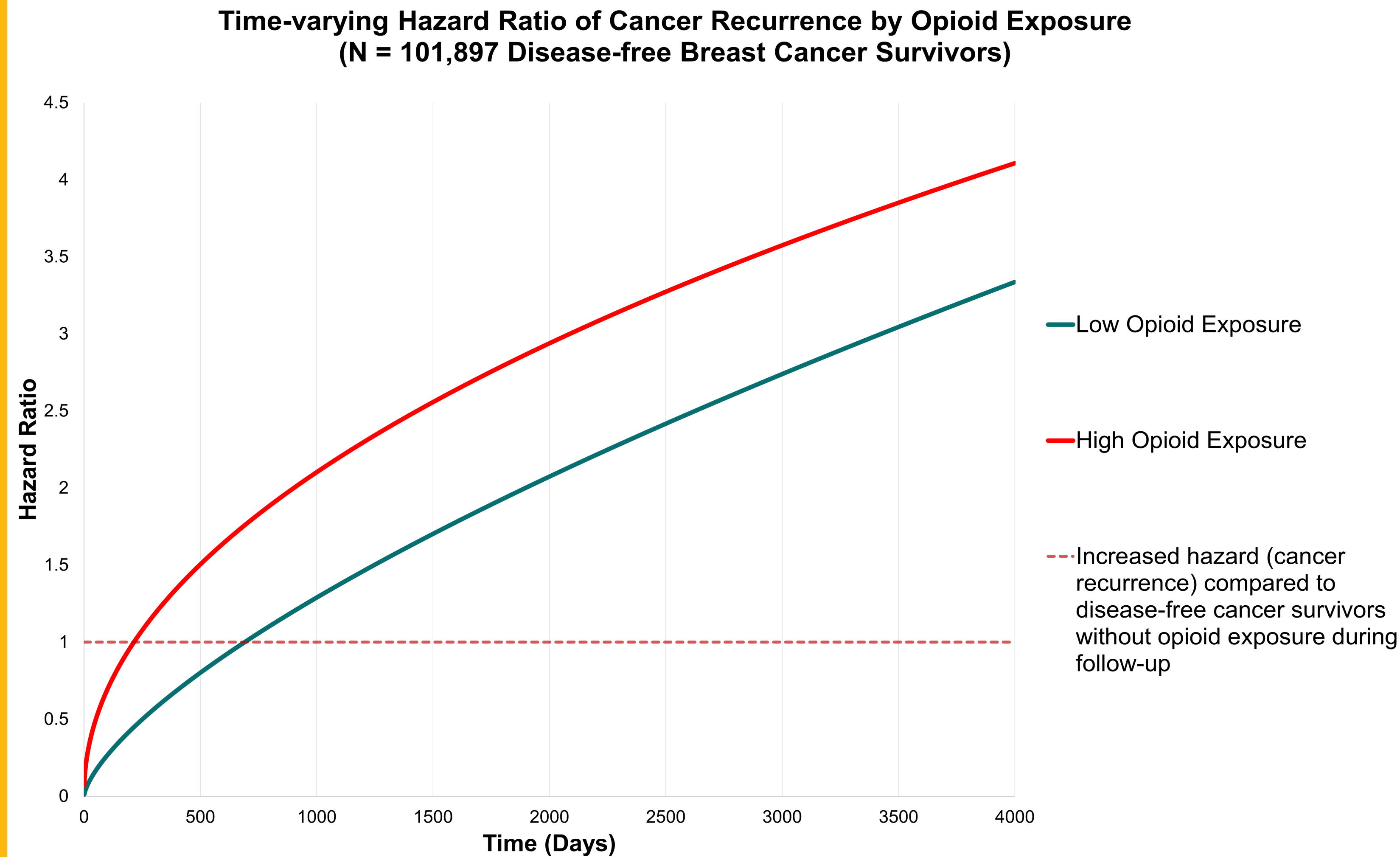
Study Design

Population	Disease-free breast cancer survivors
Control	No Opioid Use
Comparator	Persistent Opioid Use (Quartiles)
Outcome	Cancer Recurrence
Time	January 2014 – Dec 2024
Setting	United States
Data Source	IBM MarketScan
Analytical Model	Extended Cox Model



Scan the QR code for full methods, patient characteristics, and references. For questions: vieiradasilvv@vcu.edu

Figure 1. Time-varying Hazard Ratios of Cancer Recurrence by Opioid Exposure (N=101,897 Disease-free Breast Cancer Survivors)



Cancer survivors exposed to opioids exhibit an **increasing risk of cancer recurrence, that appears to be dose and frequency dependent** compared to no opioid exposure.

Methods

Opioid exposure scores were defined as a function of average daily MMEs and number of days in the follow-up period with opioids in hand, using the formulas below and categorized in top-bottom percentiles (50:50)

$$PTEO = \frac{\text{Days Exposed}}{\text{Total Number of Days of Followup}}$$

Eq. 1 - Proportion of Time Exposed to Opioids (PTEO)

$$ADMMEs = \frac{\sum \text{MMEs during period of exposure}}{\text{Days Exposed}}$$

Eq. 2 - Proportion of Time Exposed to Opioids (PTEO)

$$\text{Opioid Exposure Score} = PTEO \times ADMMEs$$

Eq. 3 – Opioid Exposure Score

An extended Cox-Proportional Hazards Model was estimated to account for changes of opioid exposure during time. Schoenfeld residuals test diagnosis was plotted to verify violation of the assumption of proportional hazards.

Results

Table 1. Cancer Recurrence Rates in Disease-Free Cancer Survivors by Opioid Use

	DFCS with Opioids N=8,503	DFCS w/o Opioids N=93,394
Recurrence	2,731 (32%)	40,041 (43%)
No Recurrence	5,772 (68%)	53,424 (57%)

Table 2. Extended Cox Hazard Model Results

Baseline Effect	Adjusted Recurrence HR (95% CI)	P-value
Low Exposure	0.011 (0.009 – 0.014)	0.000
High Exposure	0.075 (0.063 – 0.088)	0.000
Time-Varying Effect	Adjusted Recurrence HR (95% CI)	P-value
Low Exposure	1.986 (1.916 – 2.058)	0.000
High Exposure	1.621 (1.571 – 1.672)	0.000

Model was adjusted for age, region, insurance type, comorbidities, and opioid use prior to cancer diagnosis. CI: Confidence Interval; HR: hazard ratio