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Objective

To examine whether opioid tapering is associated with takotsubo cardiomyopathy (TCM) and major adverse cardiovascular events (MACE) among older Medicare beneficiaries.

Key findings

Opioid tapering increases the risk of cardiovascular outcomes such as TCM and MACE; and the risk is even greater when tapering occurs rapidly.

Implications

Cardiovascular risk should be weighed before initiating opioid tapering. Gradual, patient-centered dose reduction is preferred over rapid tapering, particularly in older adults on higher baseline doses.

Funding

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Key references

Chow SL, Sasson C, Benjamin EJ, et al. Opioid use and its relationship to cardiovascular disease and brain health: A presidential advisory from the American Heart Association. *Circulation*. 2021;144(13):e218-e232. doi:10.1161/CIR.0000000000001007
Krantz MJ, Palmer RB, Haigney MCP. Cardiovascular complications of opioid use: JACC state-of-the-art review. *J Am Coll Cardiol*. 2021;77(2):205-223. doi:10.1016/j.jacc.2020.11.002

Methods

Data source: 5% sample of Medicare fee-for-service data (2012–2020)

Study design: Case-crossover design

Population

- Medicare beneficiaries aged ≥65 with a long-term opioid therapy (LTOT) episode
- Continuous enrollment in Medicare Parts A, B, and D for the 180-day baseline window
- Excluded: Medicare Part C enrollment, hospice use, or history of cancer during the baseline window

Outcomes

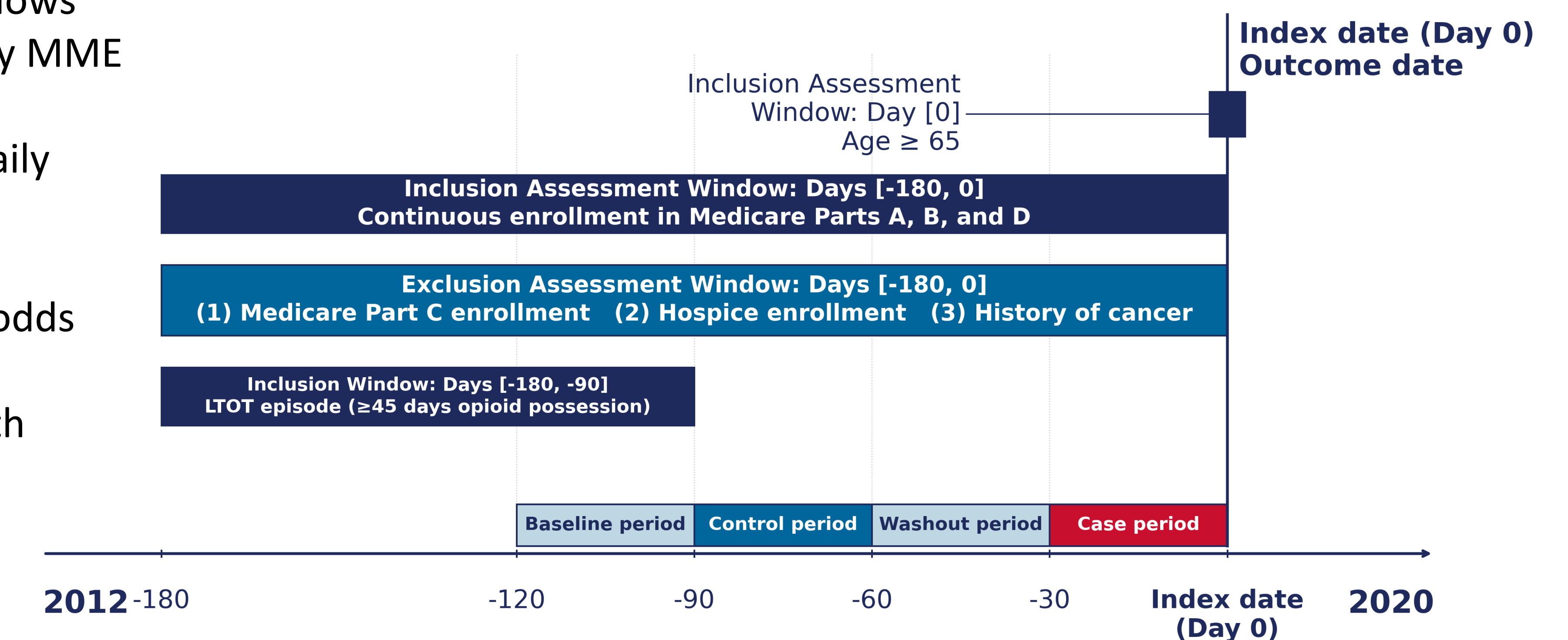
- Primary:** TCM, 3-point MACE (Myocardial infarction (MI), stroke, or cardiovascular (CV) death)
- Secondary:** Each MACE component analyzed individually

Exposure: Opioid tapering

- Calculated using mean daily morphine milligram equivalents (MME) across four 30-day windows
- Any tapering:** ≥15% reduction in mean daily MME (case vs. washout, or control vs. baseline)
- Rapid tapering:** ≥40% reduction in mean daily MME

Statistical analysis

- Conditional logistic regression to estimate odds ratios with 95% confidence intervals
- Subgroup analysis restricted to patients with baseline mean daily MME ≥50



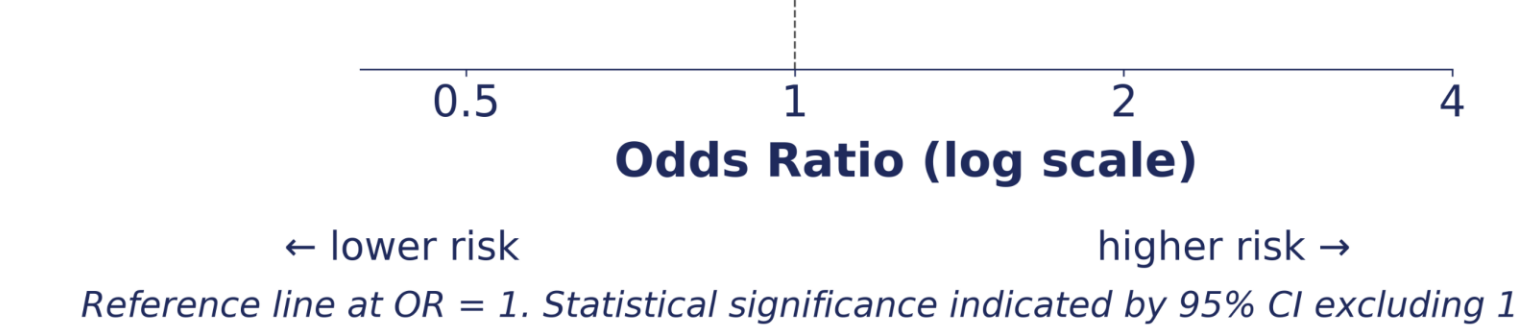
Results

- Between 2012 and 2020, 426 cases of TCM, 28,321 cases of MACE, 9,833 cases of MI, 20,544 cases of stroke, and 1,864 cases of CV death were identified.

	TCM	MACE	MI	Stroke	CV death
Age, mean (SD)	74.80 (7.00)	75.99 (8.14)	76.62 (8.29)	75.70 (7.97)	78.66 (8.67)
Female, n (%)	382 (89.67%)	19,062 (67.31%)	6,393 (65.02%)	14,039 (68.34%)	1,214 (65.13%)
White, n (%)	380 (89.20%)	24,114 (85.15%)	8,330 (84.71%)	17,522 (85.29%)	1,603 (86.00%)
CCI score, 3 and more, n (%)	326 (76.53%)	20,373 (71.94%)	8,328 (84.69%)	13,935 (67.83%)	1,744 (93.56%)
Multiple CNCP condition, n (%)	318 (74.65%)	17,662 (62.36%)	6,750 (68.65%)	12,475 (60.72%)	1,164 (62.45%)

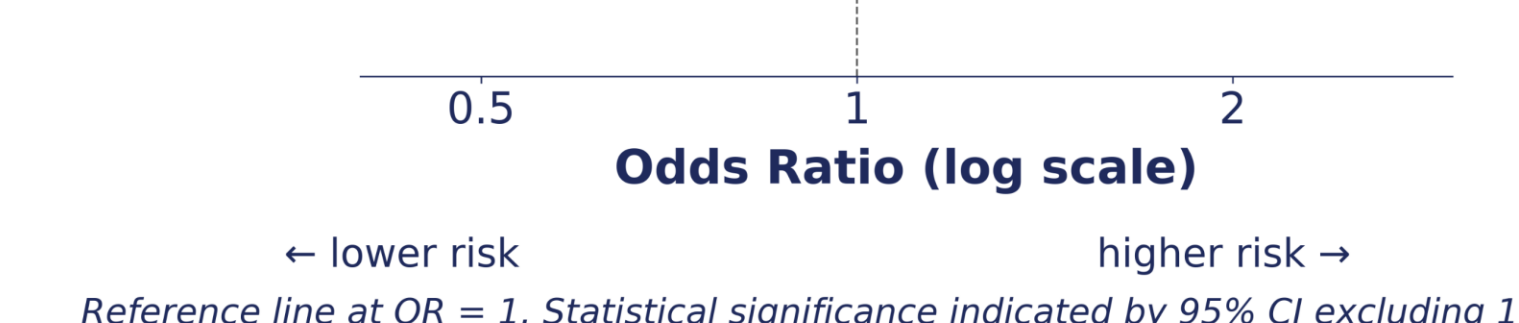
Primary Analysis: Any Opioid Tapering

Outcome	N	OR (95% CI)
TCM	426	1.55 (1.03-2.33)
MACE	28,321	1.44 (1.37-1.51)
MI	9,833	1.57 (1.44-1.71)
Stroke	20,544	1.38 (1.30-1.46)
CV death	1,864	2.26 (1.87-2.73)



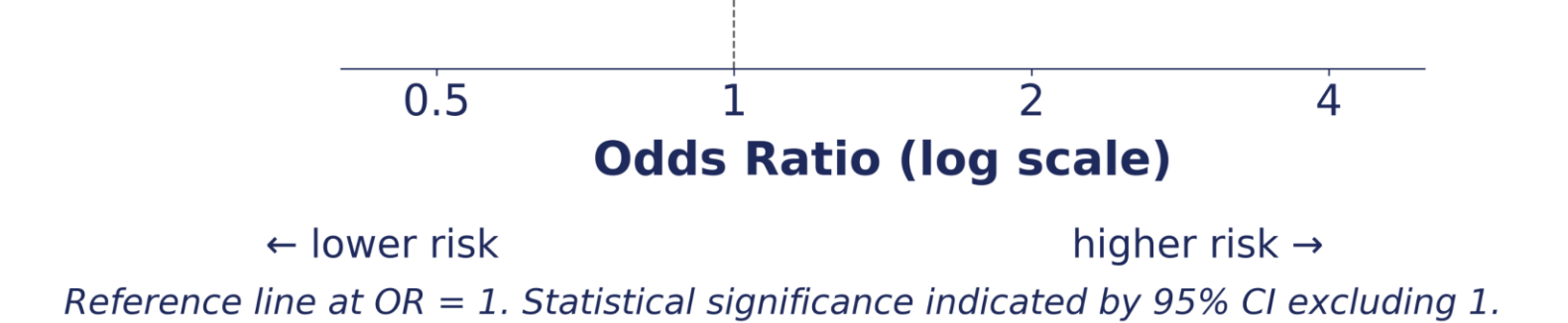
Subgroup Analysis: Any Opioid Tapering

Outcome	N	OR (95% CI)
TCM	174	0.90 (0.47-1.72)
MACE	7,658	1.17 (1.07-1.29)
MI	2,818	1.23 (1.06-1.44)
Stroke	5,603	1.16 (1.03-1.29)
CV death	492	1.36 (0.96-1.92)



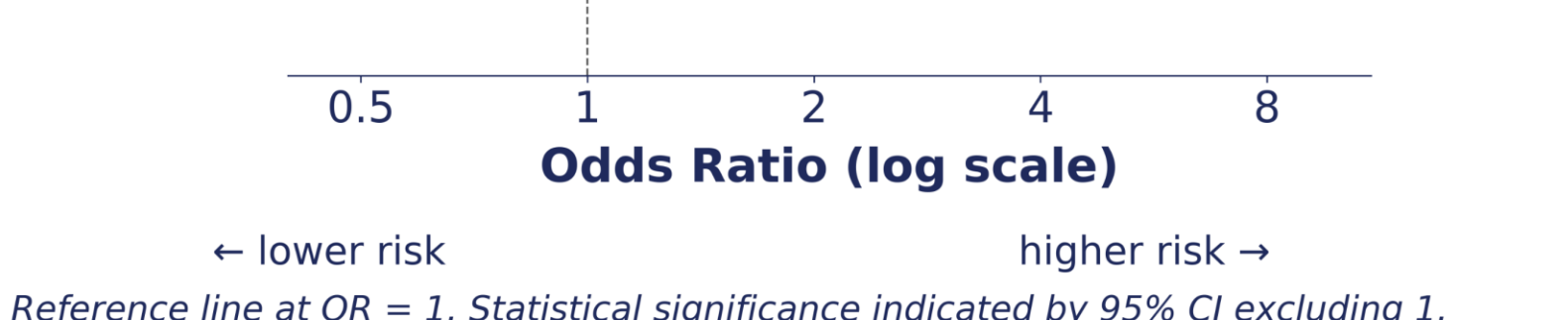
Primary Analysis: Rapid Opioid Tapering

Outcome	N	OR (95% CI)
TCM	426	2.27 (1.24-4.16)
MACE	28,321	1.92 (1.80-2.05)
MI	9,833	2.04 (1.83-2.29)
Stroke	20,544	1.85 (1.71-2.00)
CV death	1,864	3.21 (2.54-4.05)



Subgroup Analysis: Rapid Opioid Tapering

Outcome	N	OR (95% CI)
TCM	174	2.67 (0.71-10.05)
MACE	7,658	1.46 (1.27-1.69)
MI	2,818	1.69 (1.33-2.14)
Stroke	5,603	1.41 (1.19-1.66)
CV death	492	1.87 (1.21-2.89)



Discussion

- The findings of this study suggest that among older Medicare beneficiaries receiving LTOT for noncancer pain, opioid tapering was associated with increased risks of adverse CV outcomes, including TCM and MACE. Rapid tapering was associated with even greater risk.
- Our findings point to several practical considerations for clinical practice. A structured CV risk assessment should be incorporated into tapering decisions.
- For patients with established CV disease, pre-taper cardiology consultation and shared monitoring between pain management and cardiology may help mitigate CV harm.
- given the magnitude of risk observed with rapid tapering, when dose reduction is indicated, gradual, collaboratively developed tapering plans, with close clinical monitoring, may help mitigate potential CV complications and avoid the risks associated with abrupt dose reductions.

