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How long should a person continue MOUD? A recent expert review clearly recommended it to be "life-long because discontinuation of MOUD is associated with an increased risk of death". [1] *However, many patients eagerly pursue taper as a goal. The reasons for this are myriad (and often based in stigma), but we shan't digress. The question is coming closer to the forefront with long-acting buprenorphine products that make a taper physiologically easier, though not necessarily safer in the long run.*

Specific evidence to guide discussion about risk vs benefit of taper would be helpful. Is it ever less risky? After what stabilizing factors have been accrued? There is suggestion that five years of abstinence from substance use disorders in general predicts future stability[2] *but that evidence is lacking for OUD, where agonist medication is critical to stabilization. What we know about the risk of uncovering receptors occupied by medication is its association with risk of death, but that comes largely from retrospective observations that treats all discontinuation the same – regardless of time in treatment or reason for cessation.*

This paper, funded largely by NIDA, attempts to add light to this topic by looking at the question of time. It assessed survival by duration of therapy over 6years among patients with OUD treated at the VA. They found that relative to those who discontinued MOUD at 6months, continuation was associated with better survival for at least four years, perhaps longer. (Numbers were low enough after year 4 to call in to question the power to detect a difference). Further, because of methods described below, it is more likely that this study ***underestimated*** *the potential survival advantage of therapy than overestimated it. And, because the data are observational, it is subject to the possibility of unmeasured confounders (i.e., motivation, severity of disease) as the true cause of survival advantage. Finally, it does not consider other downsides to discontinuation (i.e., returns to use that are not fatal but come with significant consequences). Still, for those who plan to stop therapy, it provides a data point to share about how long we can document benefits of medication in terms of survival.*

Please read on for more details and thank you for reading!

Andrea Truncali MD MPH

Title: MOUD is associated with survival benefit for at least four years in a population of US Veterans

Citation: Evaluating the optimal duration of medication treatment for opioid use disorder. Hayes, C. J., Raciborski, R. A., Acharya, M., Noor, N. B., Nunes, E. V., & Winhusen, T. J. (2026). *Addiction*, *121*(4), 922–933.

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC12980296/

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METHODS

This was a retrospective cohort study using VA data from Oct 2010-Sept 2020. Included were patients diagnosed with OUD and receiving any MOUD filled at a VA pharmacy. Patients entered the study at initiation date (first MOUD use) and were followed until death or end of study follow up. Excluded were those who got MOUD from a non-VA pharmacy, had metastatic cancer, resided at a nursing home or hospice or had <1yr of baseline data. The analysis was not preregistered.

The **exposure of interest was duration of initial episode of MOUD and the primary outcome was all cause mortality.** Discontinuation was as commonly defined: a treatment gap >28days (from end of last rx to beginning of new). Switching to different MOUD was not considered a gap but treatment interruption *was* considered a discontinuation. This means if someone stopped treatment but resumed it later, they were still counted as having discontinued medication.

Adjustments were made for multiple variables, and the authors used the "illness-death modelling framework" to analyze the data. This is different from the Cox proportional hazard model which is often used to compare survival while adjusting for potential confounders. With the illness-death model, one can model different events without censoring/treating them as competing events, making it useful for studying chronic disease outcomes. However, the results are not easily interpretable (doesn't give a hazard ratio) so the authors classified results into risk groups to make the findings interpretable.

Two sensitivity analyses were conducted: 1) excluding those who switched MOUD (3.2%) and 2) excluding those who resumed MOUD (42.2%).

RESULTS

Participant characteristics

As expected from a VA sample, the average age was 49 and 92.4% of the sample was male. 60.8% started on buprenorphine, 26.8% on methadone and 12.4% on injectable naltrexone. 71.9% were white, 19.1% black. See paper for more details but some additional key descriptors were: 29.0% married, 18.6% employed and 43% VA priority group 1 (highest support). 85.1% were urban and the SVI composite score was 0.54 (0-1, lowest-highest). 39.4% were unhoused. 48.5% had alcohol use disorder (AUD), perhaps explaining the high rate of naltrexone use. 59.8% had tobacco use disorder and 58.1% had another substance use disorder, 83.5% had a pain-related health condition and 19.8% had hep C. 9.6% had a psychotic disorder and 61.7% had an anxiety disorder.

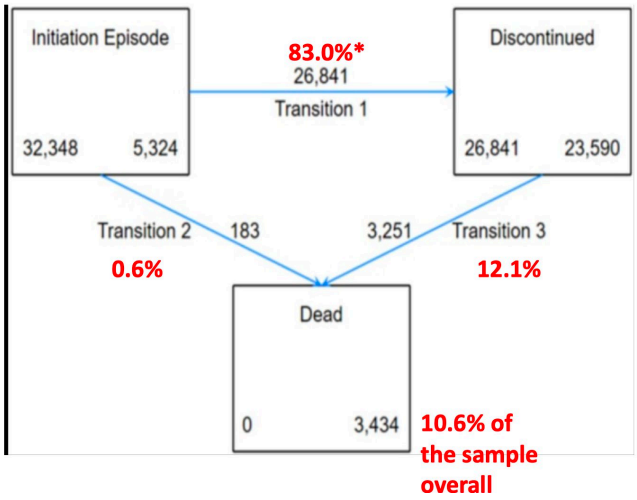
Medications and risk of discontinuation and death

	State		
Characteristics	Initiation of MOUD, *n* = 32 348	MOUD discontinuation, *n* = 26 841	Death, *n* = 3434
Type of MOUD initiated (*n*, %)			
Buprenorphine	19 666 (60.8)	14 683 (54.7)	1797 (52.3)
Methadone	8675 (26.8)	8333 (31.0)	1339 (39.0)
Extended-release naltrexone	4007 (12.4)	3825 (14.3)	298 (8.7)

Note that in the **unadjusted data**, buprenorphine and naltrexone were less represented among those who discontinued as well as among those who died, while methadone was more represented in those

groups. And, being married, white, employed, non-urban, housed and in a high VA priority group had disproportionately lower representation in the group who died, while tobacco, AUD, prior overdose, Hep C, prescription -benzodiazepine, hypnotics, or non-opioid analgesics, depression and psychosis were overrepresented among those who died. These factors did not always have a clear association with discontinuation perhaps suggesting other causes of mortality for those characteristics.

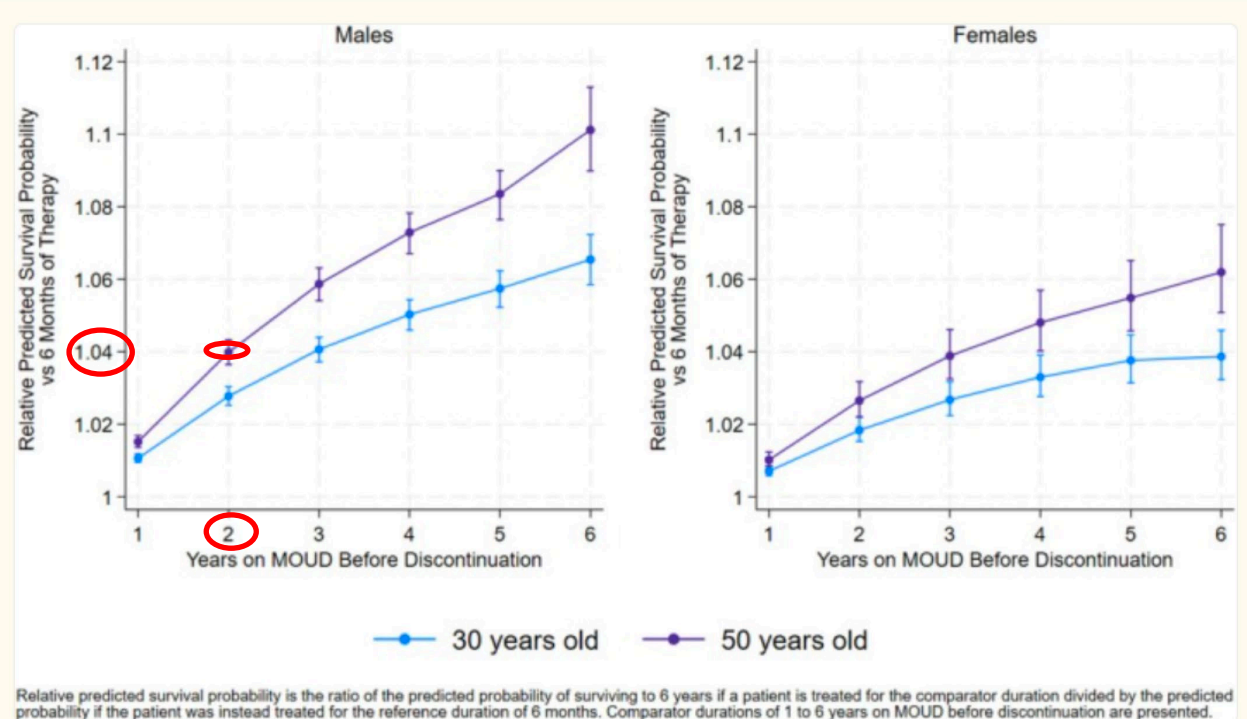
The following diagram describes patient flow:



The percentages in red are my additions and don't consider that people were measured for different periods of time but are given to provide a more tangible sense of patient outcome.

85% were followed >1 yr post initiation and 84% followed >1 yr post discontinuation. More specific follow-up was given in person-years (and less intuitive).

Main Result



Increased time on therapy came with an increase in relative survival as demonstrated for 4 sample patients: 30-year-old man and woman, and 50year old man and woman. A specific interpretation example is that the expected 6yr survival probability is 4% higher for a 50yo man who takes MOUD for 2yrs compared with 6months. The advantage loses significance at 4yrs but according to authors this may be due to small numbers beyond 4yrs. These plots /predictions are made for those without co-occurring risks and should be higher for higher risk groups.

Sensitivity analysis showed no difference in the overall trend but when those who resumed treatment (42%) were excluded, projected survival was lower (as they were likely inflating the survival rate due to protection with medication).

CONCLUSION

In this population of Veterans new to MOUD treatment, treatment up to 4years was associated with increased relative survival. Gains were clearly demonstrated up to 4years with possible impact beyond (limited by power).

COMMENTARY

Internal validity *(how likely are the study results what they appear to be for the study group)*

Overall, this paper looked at survival over a substantial time period and used valid outcome measures (such as MOUD codes, prescription and all-cause mortality data).

As with all observational studies, **we wonder if the survival impact was confounded by factors not easily captured** in this database, i.e., motivation, level of function, severity of disease. For example, a person with less severe disease might be likely to live longer because of those advantages but here that impact is all attributed to MOUD.

As above, exposure and outcome data are likely reliable, however, people could have received treatment outside of the VA - authors estimate this as low probability, and if it occurred, it would make discontinuation appear safer/reduce apparent benefit of treatment.

One challenging aspect of this trial is the modeling that makes the results non-intuitive. It is also important to note that the analysis was not outlined a priori.

Overall, it seems **most likely that the study underestimated impact**: those who resumed treatment were considered discontinued (sensitivity analysis suggested some impact on strength of findings), and there was the suggestion that higher risk people might have more benefit but they used lowest risk individuals (no co-occurring dos) as reference participants. It seems like this could have been modeled in the supplement and it is curious why it wasn't.

External validity *(how can these results be applied beyond the study)*

This population is more male, older and higher risk than the broader OUD population. They had low employment and a high prevalence of being unhoused. Authors limited the impact of this by reporting survival gains as relative rather than absolute and stratifying by age and sex.

This study **did not have the capacity to identify reasons for discontinuation.** And perhaps most critical in applying this to practice is that while **survival is a major consideration, it is not the only outcome of interest in weighing treatment decisions**. Other data suggests impact on reduced ED visits, inpatient utilization and overdose; and few data capture the impact of a non-fatal return use on the quality of life for those with OUD, their families and community.

REFERENCES

1. Harris, M. T. H., Weinstein, Z. M., & Walley, A. Y. (2026). Medications for Opioid Use Disorder, Opioid Withdrawal, and Opioid Overdose: A Review. *JAMA*, *335*(11), 986–998. https://doi.org/10.1001/jama.2025.26348

2. DuPont, R. L., Compton, W. M., & McLellan, A. T. (2015). Five-Year Recovery: A New Standard for Assessing Effectiveness of Substance Use Disorder Treatment. *Journal of substance abuse treatment*, *58*, 1–5. https://doi.org/10.1016/j.jsat.2015.06.024