

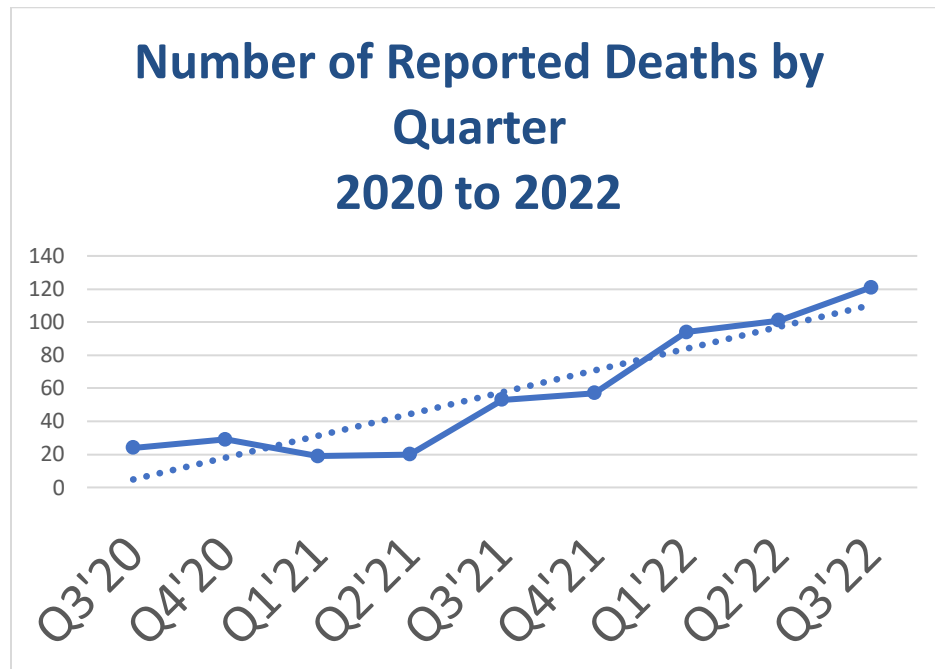
American Clinicians Academy on Medical Aid in Dying

www.ACAMAID.org

DDMAPh Update, 10-11-22. Posted to the Academy Listerve.

We have important new information about the use of the medication regimen, DDMAPh. (Diazepam, Digoxin, Morphine, Amitriptyline, Phenobarbital.)

But first, a milestone: The Academy's aid-in-dying patient data reports for DDMAPh exceeded 500 last month, now at 521 cases, with highly detailed information. And the rate at which clinicians are reporting results to the Academy is climbing steadily.



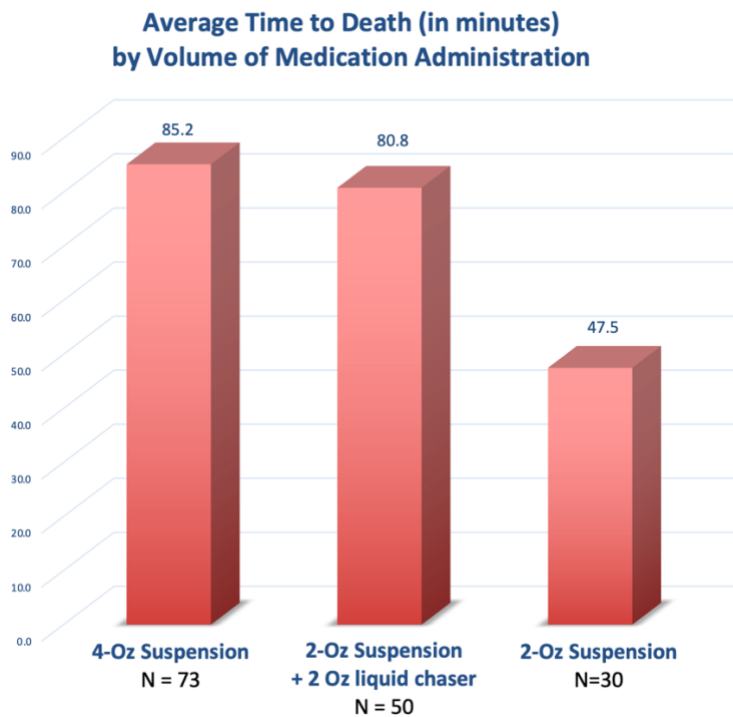
Thank you!! to all who file your anonymized patient death data. We hope more clinicians will join in, to help us better understand how these medication protocols are working. It takes 2 minutes. To contribute: (Most efficiently, soon after you've completed an aid-in-dying death): <https://www.acamaid.org/datareport/>

Now, the clinically significant news:

In following the data reports, we noticed in early 2022 that some clinicians were using a medication mixture volume of 2 ounces instead of the usual 4. Others were using an initial 2-ounce volume, followed by 2 ounces of water or thin apple juice (a "chaser" to match the total gastric volume of 4 ounces).

The rationale for both 2-ounce protocols was that the patient could more easily ingest the full amount of medications, and the shorter ingestion time might decrease the burning sometimes experienced with DDMAPh. But there was no actual data to show whether these different volumes of administration were equal, better, or inferior to each other. So we adjusted our data-entry forms to get more detailed information. We've now had 80 reports using the two-ounce mixtures.

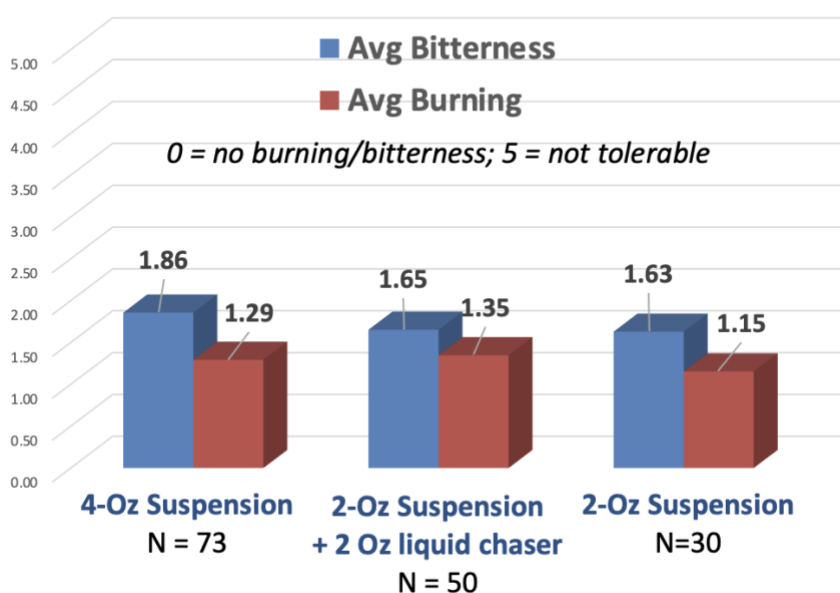
My personal hypothesis was that the 2-ounce regimen (without the chaser) would be too thick, impeding duodenal absorption and risking longer times to death. I was wrong.



We're seeing (so far) a remarkably shorter time to death with the 2-ounce mixture (not followed by the chaser). And even though the N of 30 is low, the difference is so profound that the calculated P value is 0.058, just a hair shy of the generally accepted $P < 0.05$ level of "statistical significance" (a 95% chance that the results are not random).

This wouldn't matter much if the increased concentration of the two-ounce mixture caused more burning or a more severely bitter taste. But it doesn't.

Average Bitterness & Burning by Volume of Medication Administration



From the data we have so far:

- The 2-ounce volume is leading to more rapid and reliable times to death than the 4-ounce volume (about a 44% improvement).
- This improvement is not compromised by increased bitterness or burning.
- The 2 ounces followed by a two-ounce water/juice chaser has no significant advantage.

What do I think is happening? These are only guesses, the kinetics of megadose pharmacology haven't been suitably studied. First, the "thicker" medication concentration at two ounces compared to four isn't so thick that gastric and duodenal peristalsis can't handle it. And it's not so thick that the duodenal mucosa is not exposed to flowing medications. (My fear had been that once the duodenum sucked out the water, which it does quite rapidly, the medications still there would be the consistency of toothpaste, not able to flow across the mucosal lining. Again, I was wrong. That's why I love data instead of conjecture.)

Then, there seems to be no increase and maybe a slight improvement in burning and bitterness — most likely because with a two-ounce ingestion there's less time of oropharyngeal/esophageal mucosal exposure to the meds (and a quicker time to the post-ingestion sorbet that most clinicians are using). So even though the two-ounce meds are more concentrated, patients reported slightly less burning/bitterness.

Again, these are only guesses, we don't have data to prove the mechanisms of what's happening — only that it's happening.

Why is this clinically significant?

- Many patients struggle to get four ounces of medications down in the two-minute allotted time before they are likely to fall asleep. We've needed an easier/quicker oral administration method. This new data suggests that outcomes with the lower volume are probably better and almost certainly not inferior to the higher volume.
- The time-to-death improvement of 44% comparing 2 ounces to 4 is welcome. We'll keep following new data as it comes in to see if this benefit holds true.
- The slight improvement in bitterness/burning is an unexpected benefit, but I'm not convinced it's real (the measurement tool isn't very fine, and the difference we're seeing isn't major).

Recommendations: The Academy is, at this time, *not making a specific recommendation*. We'll keep gathering data to see if the early results hold up with more patient reports. Meanwhile, **it is up to each clinician to decide — based on the preliminary data above — the best protocol to use for each individual patient.**

And whatever volume of mixed medications you use, we need your data to better understand how it works. Again, <https://www.acamaid.org/datareport/>.

Thank you!! to Angelique Loscar, MBA — the Academy data maven. And Aja DeWolf-Moura, who analyzed the statistical significance.

And thank you all for your diligence and caring. Send in your data!! It's essential to what we do.

Looking forward,

Lonny

Lonny Shavelson, MD

Chair

American Clinicians Academy on Medical Aid in Dying