Development of Novel Endpoints for Clinical Trials in Substance Use Disorder

Chairs:

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Disclosures

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Innovation in Substance Use Disorder Therapeutics Development
Reasons & Needs

- **Opioid Crisis** in the United States was declared a public health emergency in 2017
- **Overdose (OD) deaths** are still increasing exponentially: more than 10 times increase from 2009 to 2019 (CDC data): nearly 450,000 opioid OD deaths alone

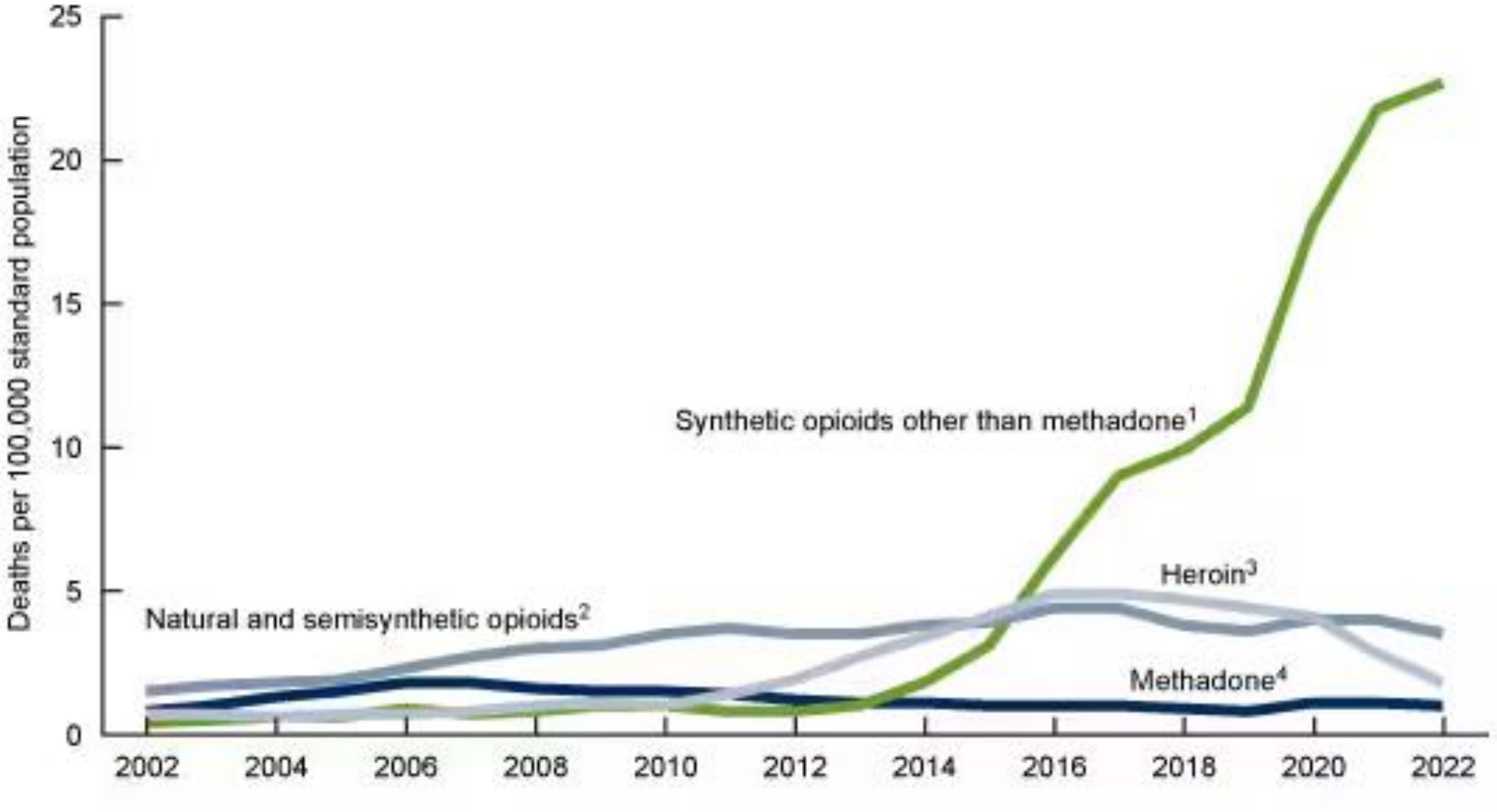
In the meantime, on the clinical front:

- **Dichotomous primary endpoint of total abstinence** is still the main clinical outcome used by the FDA (except for alcohol use disorder): hard to achieve, high technical risk; needs to be confirmed by urinalysis, while it is not equated with what patients themselves see as beneficial for their treatment needs
- **Harm reduction model**: Recently the US regulators became open to drug use decrease as a primary endpoint. However, they want to see that decreased drug use endpoint correlates with a salutary benefit for a patient, reflecting the FDA endpoint definition of "how patients feel, function, or survive". Demonstrating such a correlation presents a separate issue for clinical drug and therapeutics development
- **Heterogeneity of the SUD population** is another issue, especially in the SUD population defined by DSM-5

And so,

- **None** of the ten largest pharmaceutical companies have active addiction medicine programs or drug candidates, and the pharmaceutical industry as a whole has only pursued minimal substance use-focused drug development According to the Biotechnology Innovation Organization (BIO)

Deaths from Opioids



SOURCE: National Center for Health Statistics, National Vital Statistics System, mortality data file.
https://www.cdc.gov/nchs/products/databriefs/db491.htm#fig4

Slow Modernization of Regulatory Approach – Harm Reduction Model – Decrease in Drug Use Pattern, but More is Needed

- Need to shift from abstinence-based, response/remission binary endpoints to continuous endpoints
- Endpoints can mirror those used for other mental disorders to assess efficacy via rating scales, e.g., symptom improvement rating scale
- Craving: Endpoint, Measurement, Indication. European findings &novel perspective
- Innovative clinical trial statistics and trial designs can be applied to the Substance Use Disorder field
- Roadmap for the future, universal outcomes across SUD
  - Benefits of the Drug Development Tool (DDT) FDA/CDER pathway for clinical trials in SUD (Alcohol Use Disorder) are awaited to be seen.
  - Novel endpoint for alcohol use disorder received the DDT Qualification Letter on Jan14, 2025 after a multi-year effort