Analytical Plan for Effects of harm reduction strategies on mortality from opioid overdose in Palm Beach, US: retrospective cohort

DOCUMENT: SAP-2022-038-MB-v01

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2022-12-11

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Document version

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01	Initial version

1 ABBREVIATIONS

- CI: confidence interval
- HR: hazards ratio
- HRS: harm reduction strategy
- OD: overdose
- SD: standard deviation

2 CONTEXT

2.1 Objectives

Estimate the mortality rates of patients admitted for any opioid-related overdose under various harm reduction strategies in Palm Beach county, US.

2.2 Hypotheses

Different harm reduction strategies are associated with varying mortality rates in patients admitted for opioid OD in Palm Beach county.

3 DATA

3.1 Raw data

Upon study start the raw data will be collected in a raw table, that will be processed before analysis. The raw dataset to be collected will have 3 variables collected.

This dataset will include the dates of entry and exit of the cohort, or the date of hospital admission and the date where the endpoint was reached (either an event, or hospital

discharge). Each row represents all information collected from a single study participant, and each participant included will require a unique study ID to allow tracking of their status across the study period. Table 1 shows the structure of the raw dataset.

Table 1 *Raw dataset structure.*

id	date_entry	date_exit	outcome	hrs	age	sex	race	employment
1								
2								
3								
…								
N								

The outcome should be recorded as a binary variable: either the study participant reached the endpoint (death) or they reached the end of study period without experiencing the event. This information can be recorded in either text form (eg, yes/no), or an indicator (death = 1, end of observation time or discharge = 0).

Exposure (HRS) and all comorbidities should be recorded as binary variables, whenever possible, or in categorical form.

For categorical variables the researcher should choose a single standardized category label set, without differentiation of upper case / lower case between observations of the same label (e.g. ABC, Abc). Any comorbidity included in the data should be recorded as a binary variable, whenever possible.

3.2 Analytical dataset

Time under observation in the cohort will be calculated as the difference between the dates of entry and exit of the cohort with calendar accuracy. Time will be measured in days for analysis.

All variables in the analytical set will be labeled according to the data dictionary for the preparation of production-quality results tables and figures.

4 STUDY PARAMETERS

4.1 Study design

Retrospective cohort.

4.2 Inclusion and exclusion criteria

Patients that were admitted for OD with any opioid in Palm Beach county.

4.3 Exposures

Harm reduction strategies. One HRS will be chosen as the reference strategy and the mortality rate under all other HRS will be calculated relative to the reference category, thus effectively acting as the control category. Once the data is collected and all HRS are known, this reference should be specified prior to analysis.

If no reference category is chosen based on relevance, the first in alphabetical order will be used.

4.4 Outcomes

Specification of outcome measures (Zarin, 2011):

1. (Domain) Mortality of OD patients
2. (Specific measurement) Death
3. (Specific metric) Time to event
4. (Method of aggregation) Hazard ratio

Primary outcome

Mortality rate of opioid-related OD in Palm Beach county.

4.5 Covariates

HR of death under various HRS will be adjusted for the following covariates.

- age (numeric)
- sex (binary)
- race (categorical)
- employment status (categorical)

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

The epidemiological profile of the study participants will be described. Demographic (sex, age, race and employment status) will be described as mean (SD) or as counts and proportions (%), as appropriate. The distributions of participants' characteristics will be summarized in tables and visualized in exploratory plots.

5.1.2 Inferential analyses

All inferential analyses will be performed in the statistical models (described in the next section).

5.1.3 Statistical modeling

Mortality rates will be estimated with the Cox regression model.

Two models are planned to be created to evaluate the impact of the HRS in the mortality rate. A simpler univariate model including only the exposure will be created to serve as a base of comparison for the main model. The main model will adjust the HR between mortality and HRS by controlling for age, sex, race and employment status of the participants included in the analysis.

No variable selection is planned for this analysis. It is assumed that the variables included in the main model to control for confounding and bias were selected based on literature sources and clinical relevance. If the analysis suffers from lack of statistical power due to poor sample variability, then this analysis plan will be revised.

5.1.4 Missing data

No missing data imputation will be performed. All evaluations will be performed as complete case analyses.

5.2 Significance and Confidence Intervals

All analyses will be performed using the significance level of 5%. All significance hypothesis tests and confidence intervals computed will be two-tailed.

5.3 Study size and Power

N/A

5.4 Statistical packages

This analysis will be performed using statistical software R version 4.2.1.

6 OBSERVATIONS AND LIMITATIONS

Recommended reporting guideline

The adoption of the EQUATOR network (http://www.equator-network.org/) reporting guidelines have seen increasing adoption by scientific journals. All observational studies are recommended to be reported following the STROBE guideline (von Elm et al, 2014).

7 REFERENCES

- **SAR-2022-038-MB-v01** – Effects of harm reduction strategies on mortality from opioid overdose in Palm Beach, US: retrospective cohort
- Zarin DA, et al. The ClinicalTrials.gov results database – update and key issues. N Engl J Med 2011;364:852-60 (https://doi.org/10.1056/NEJMsa1012065).
- Gamble C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337–2343 (https://doi.org/10.1001/jama.2017.18556).
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014 Dec;12(12):1495-9 (https://doi.org/10.1016/j.ijsu.2014.07.013).

8 APPENDIX

This document was elaborated following recommendations on the structure for Statistical Analysis Plans (Gamble, 2017) for better transparency and clarity.

8.1 Availability

All documents from this consultation were included in the consultant's Portfolio.

The portfolio is available at:

https://philsf-biostat.github.io/SAR-2022-038-MB/