Analytical Plan for Impact of harm reduction strategies on mortality from opioid overdose in Palm Beach, US: case-control study

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TABLE OF CONTENTS

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Document version

Version	Alterations
01	Initial version
02	Data, outcome, study design, covariates, statistical analysis, missing data

1 ABBREVIATIONS

- CI: confidence interval
- HRS: harm reduction strategy
- MAT: medication assisted treatments
- OD: overdose
- OR: odds ratio
- SD: standard deviation

2 CONTEXT

2.1 Objectives

To assess whether two harm reduction strategies are associated with different mortality prevalence rates in patients admitted for any opioid-related overdose in Palm Beach county, US.

2.2 Hypotheses

Harm reduction strategies are associated with different prevalence of mortality in patients admitted for opioid-related OD in Palm Beach county.

3 DATA

3.1 Raw data

The original data base had 12 variables collected on 385 observations.

3.2 Analytical dataset

Individual participants included in the study were sampled between 2 and 5 times. The OD events were indexed sequentially, and the last index per participant was used for inclusion in the analytical dataset (see section 4.2).

After the descriptive analysis, a few categorical variables were collapsed into fewer categories. Employment status was simplified for analysis into “Retired”, “Employed” and “Not Employed” which was defined as the reference category. “Students” were aggregated into “Not Employed” and “Disabled” were aggregated into “Retired” for analysis. Race was simplified into “Black”, “Other” and “White” which was defined as the reference, due to its higher occurrence in the sample. “Turki” was aggregated into “Other” for analysis.

After the cleaning process 8 variables were included in the analysis. The total number of observations excluded due to incompleteness and exclusion criteria will be reported in the analysis. Table 1 shows the structure of the analytical dataset.

Table 1 *Analytical dataset structure after variable selection and cleaning.*

id	exposure	outcome	gender	race	ethnicity	narcan_discharge	employment
1							
2							
3							
…							
N							

All variables in the analytical set were labeled according to the raw data provided and values were labeled according to the data dictionary for the preparation of production-quality results tables and figures.

4 STUDY PARAMETERS

4.1 Study design

Case-control retrospective study.

4.2 Inclusion and exclusion criteria

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

Individual participants included in the study were sampled between 2 and 5 times. In order to assess mortality risk, only the last observation available for each participant was included in the analysis.

4.3 Exposures

Two harm reduction strategies (MAT and substance abuse facilities) will be compared to no exposure to any HRS.

4.4 Outcomes

Specification of outcome measures (Zarin, 2011):

1. (Domain) Mortality of OD patients
2. (Specific measurement) Death
3. (Specific metric) End-value
4. (Method of aggregation) Odds

Primary outcome

Odds of dying from opioid-related OD in Palm Beach county.

4.5 Covariates

OR of mortality under various HRS will be adjusted for the following covariates.

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

Age was not available in the data to use in the adjustment of the association effects.

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

The epidemiological profile of the study participants will be described. Demographic and clinical characteristics 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

The OR of mortality for each HRS will be estimated from a logistic regression model. The model will adjust the OR between mortality (see section 4.4) and HRS (section 4.3) by controlling for age, sex, race and employment status of the participants included in the analysis (section 4.5).

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.

5.1.4 Missing data

Data on the exposure and employment of cases were not available in the raw dataset. A Multiple Imputation by Chained Equations algorithm (Van Buuren, 2018) will be run on the dataset in the hope of estimating usable imputed values for these variables based on common characteristics from other variables available in the data.

As per the client's request, no further examination will be done on assumptions of the distribution of missingness nor the goodness of fit of the imputation model. The algorithm will be run with default parameters set in the MICE package version 3.15.0.

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 4.3.0.

6 OBSERVATIONS AND LIMITATIONS

Recommended reporting guideline

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

In particular when a retrospective study is conducted using hospital records, it is recommended that the RECORD extension of the STROBE guideline is considered (Benchimol et al, 2015).

7 REFERENCES

- **SAR-2023-021-MB-v01** – Impact of harm reduction strategies on mortality from opioid overdose in Palm Beach, US: case-control study
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- Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM; RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015 Oct 6;12(10):e1001885 (https://doi.org/10.1371/journal.pmed.1001885).
- Van Buuren, S. (2018). Flexible imputation of missing data. CRC press.

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/

8.2 Associated analyses

This document is part of a larger project and is supported by other documents, linked below.

Impact of harm reduction strategies on mortality from opioid overdose in Palm Beach, US: case-control study

https://philsf-biostat.github.io/SAR-2023-021-MB/