

JENNIFER THOMPSON, MPH @jent103 • jennifer.l.thompson@vanderbilt.edu
RAMEELA CHANDRASEKHAR, PHD
MAYUR PATEL, MD, MPH

HANDLING BIAS CAUSED BY MISSING DELIRIUM ASSESSMENTS

MOTIVATING EXAMPLE: RETROSPECTIVE COHORT FROM EHR

EXAMPLE: TRAUMATIC BRAIN INJURY COHORT

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1,383 (52%)

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Compared to patients with
complete data, patients with no
assessments are:

- ▶ older
- ▶ less “injured”
- ▶ less time on MV
- ▶ more likely to be discharged
home; less likely to go to rehab

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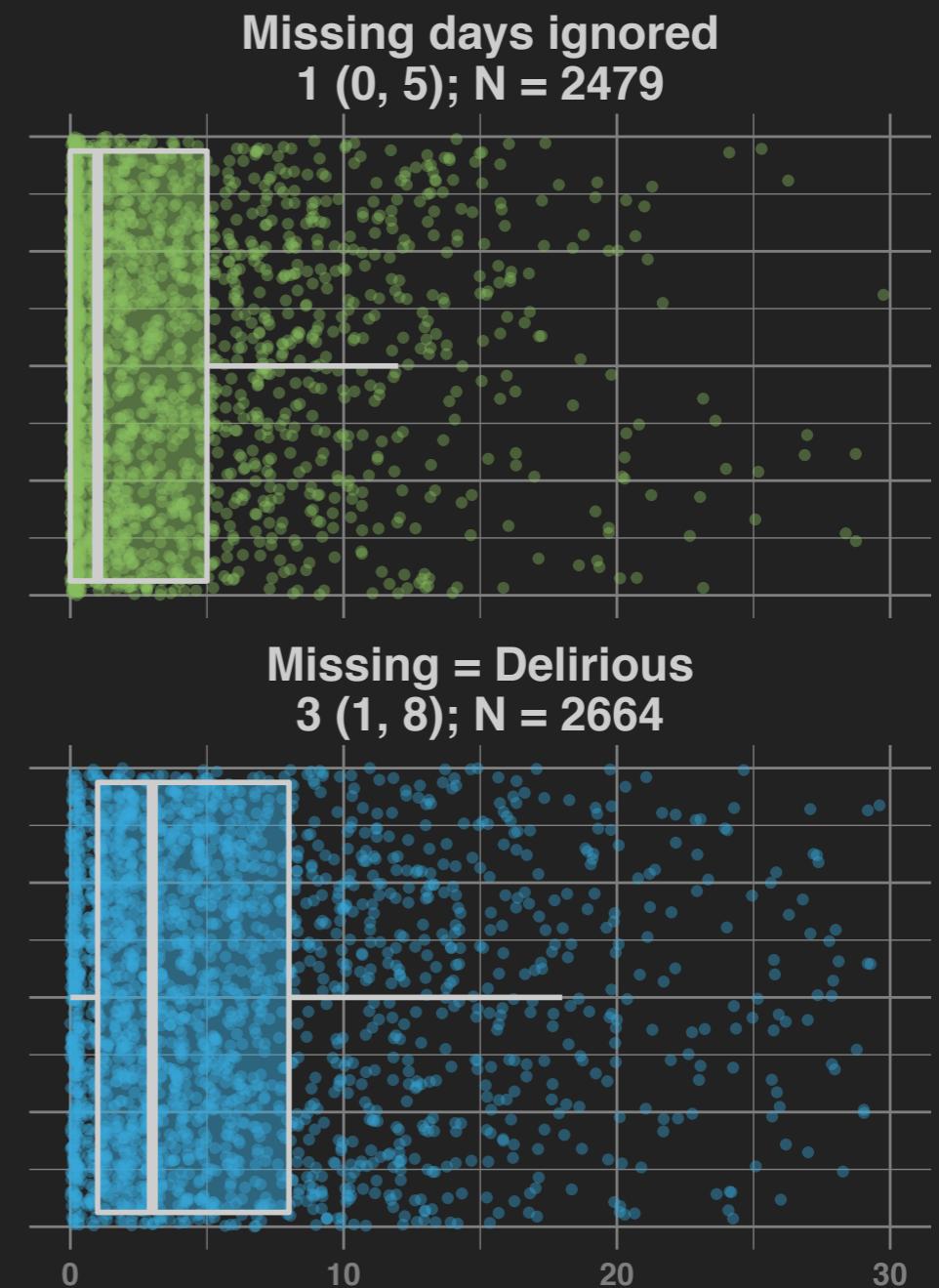
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- ▶ Value of exposure differs greatly according to how we treat hospital days with missing assessments

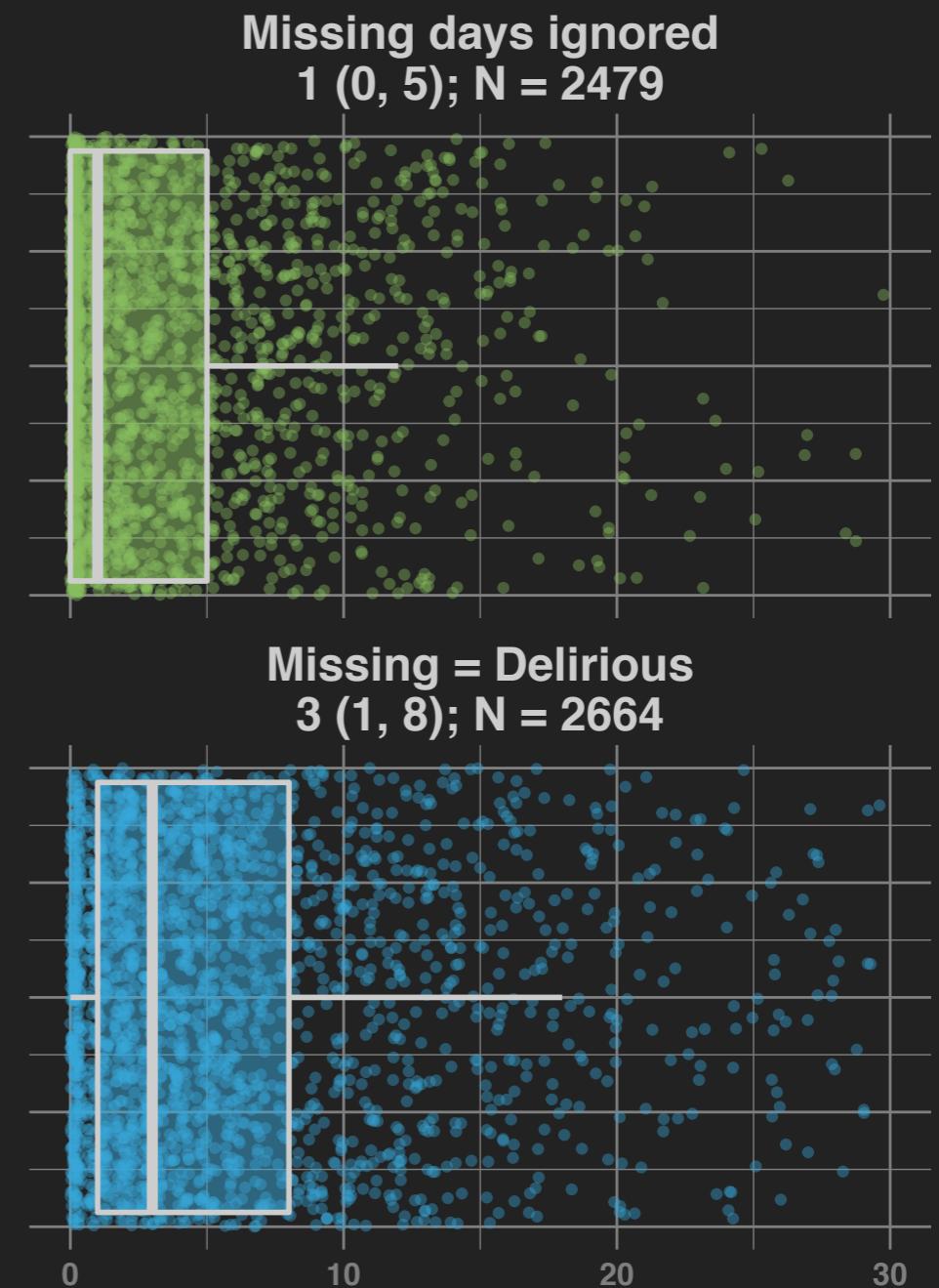
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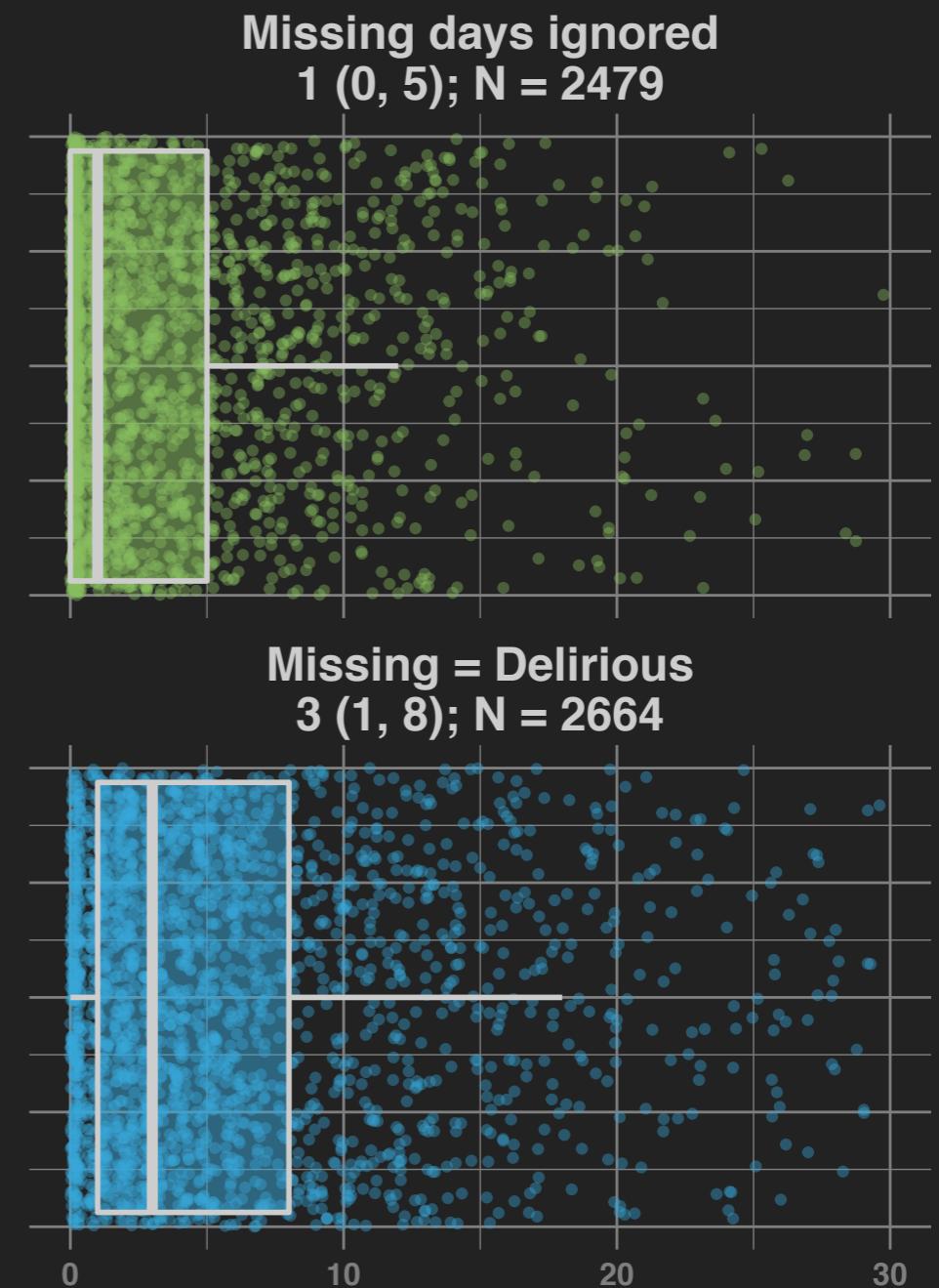
EXAMPLE: TRAUMATIC BRAIN INJURY COHORT

- ▶ Assume main exposure is duration of delirium during index hospitalization
- ▶ Value of exposure differs greatly according to how we treat hospital days with missing assessments
- ▶ Truth is probably between these extremes

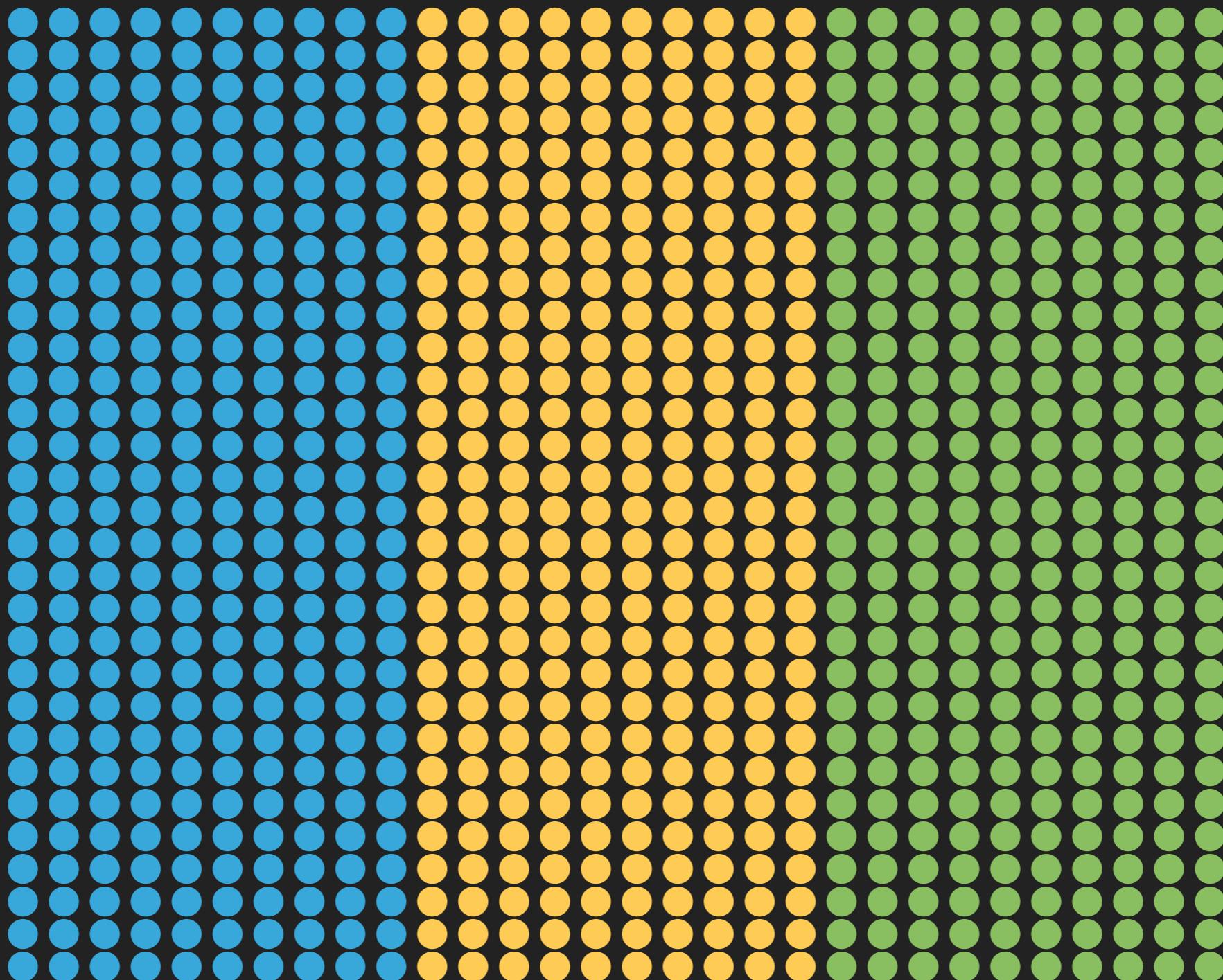


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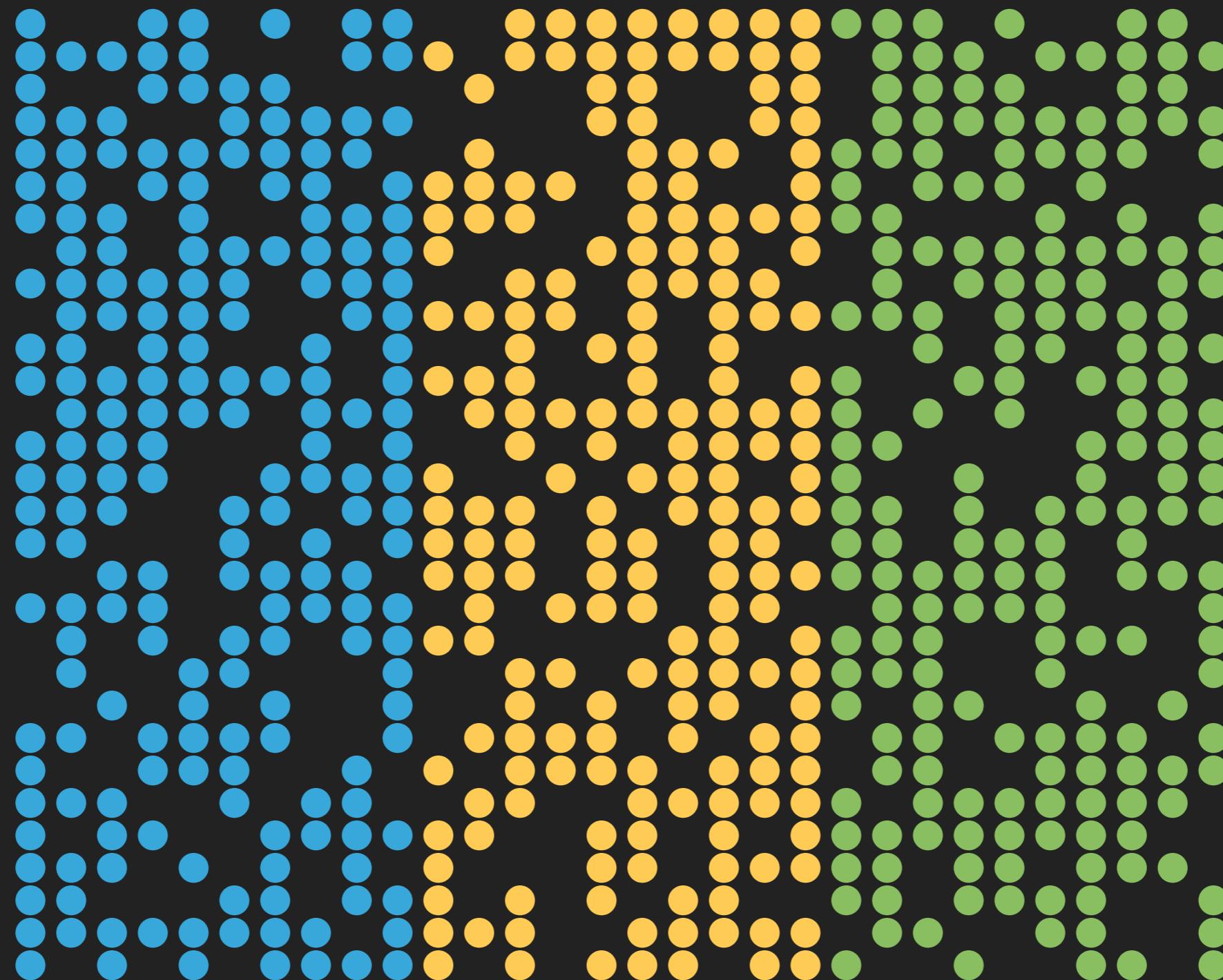
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- ▶ Value of exposure differs greatly according to how we treat hospital days with missing assessments
- ▶ Truth is probably between these extremes
- ▶ How we handle this matters: We're afraid of getting **biased results**



TYPES OF MISSING DATA



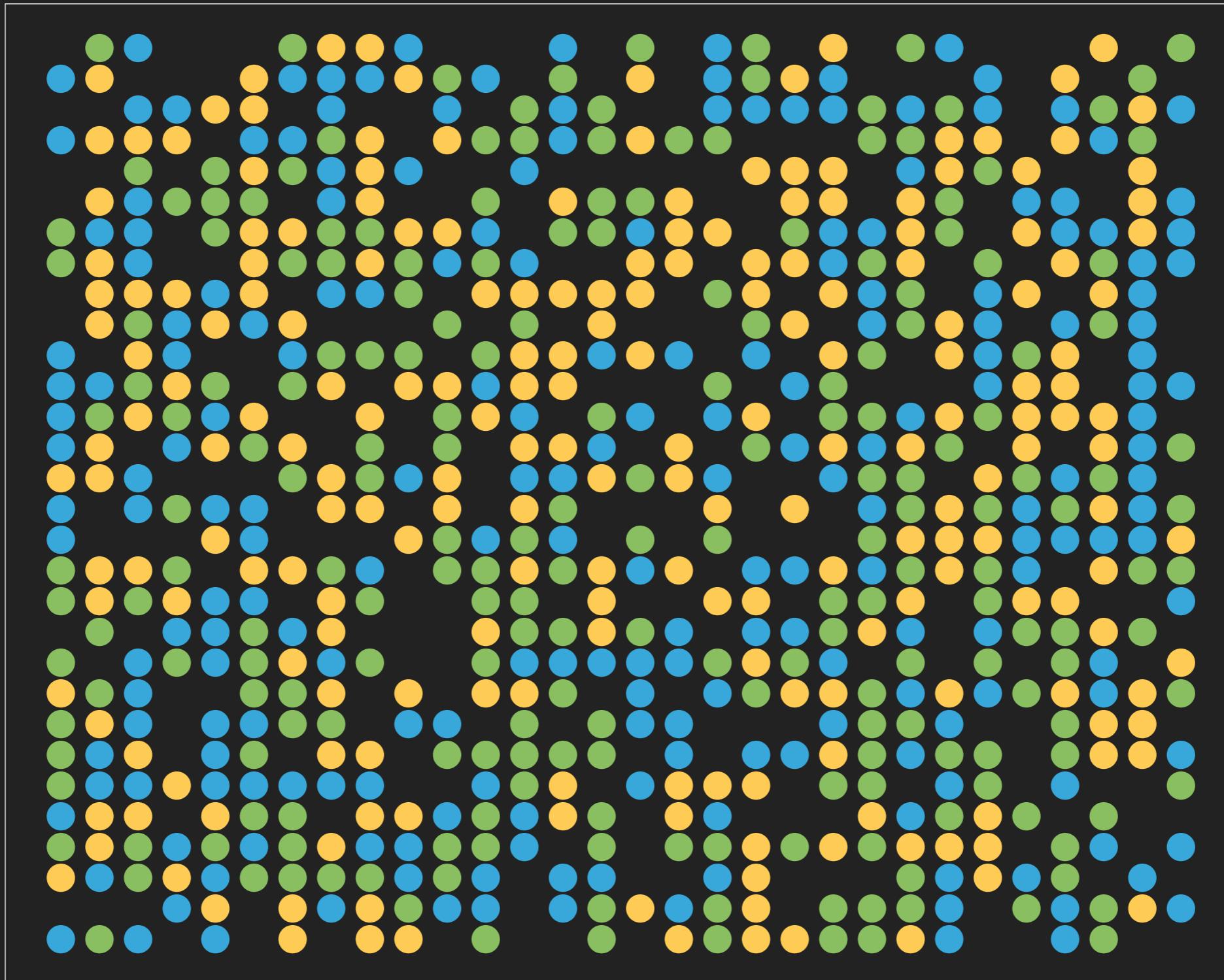
MISSING COMPLETELY AT RANDOM (MCAR)



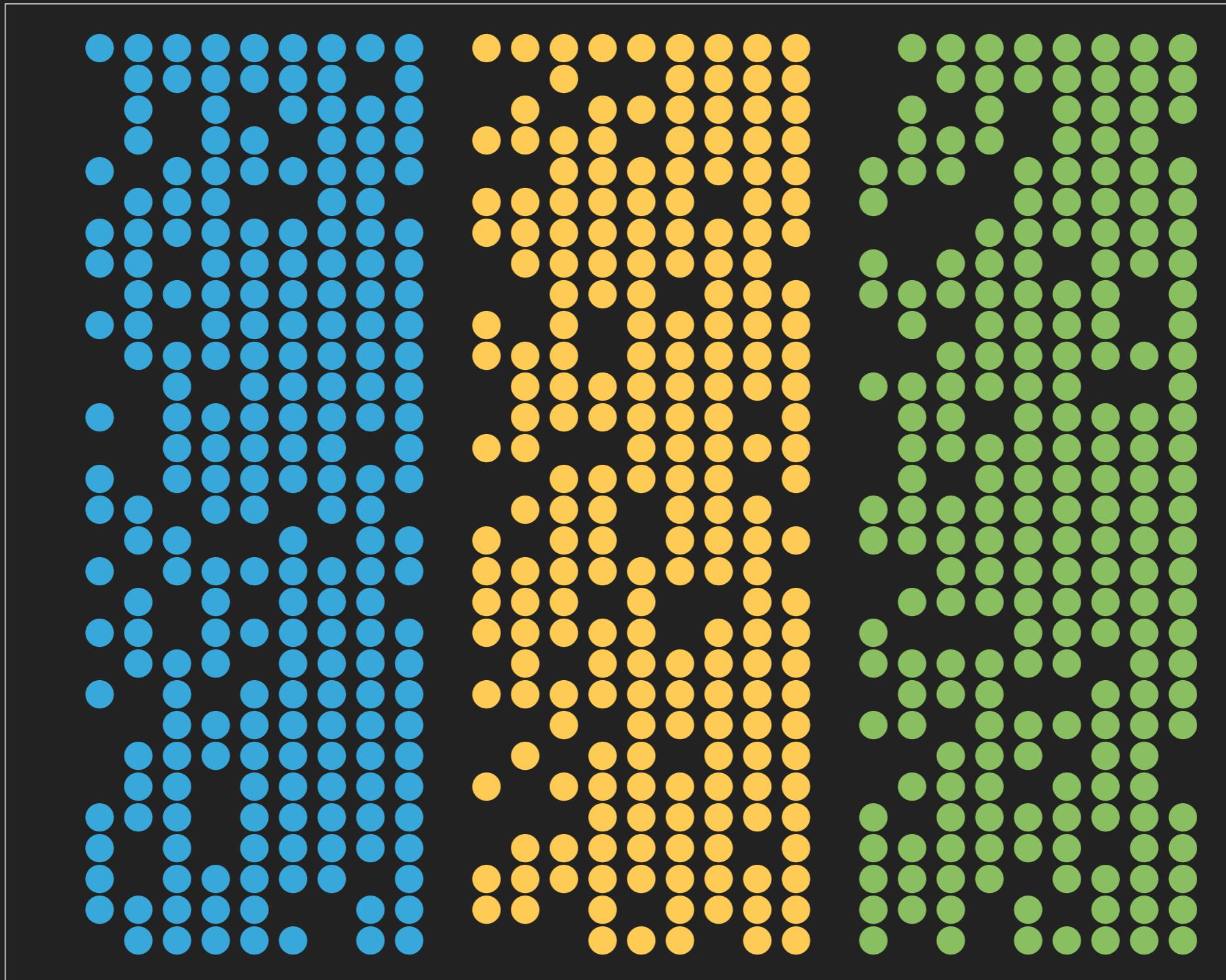
MISSING AT RANDOM (MAR)



MISSING NOT AT RANDOM (MNAR)



MISSING NOT AT RANDOM (MNAR)



EXAMPLE OF BIAS: MODIFYING BRAIN-ICU

Link: Full BRAIN-ICU manuscript, NEJM

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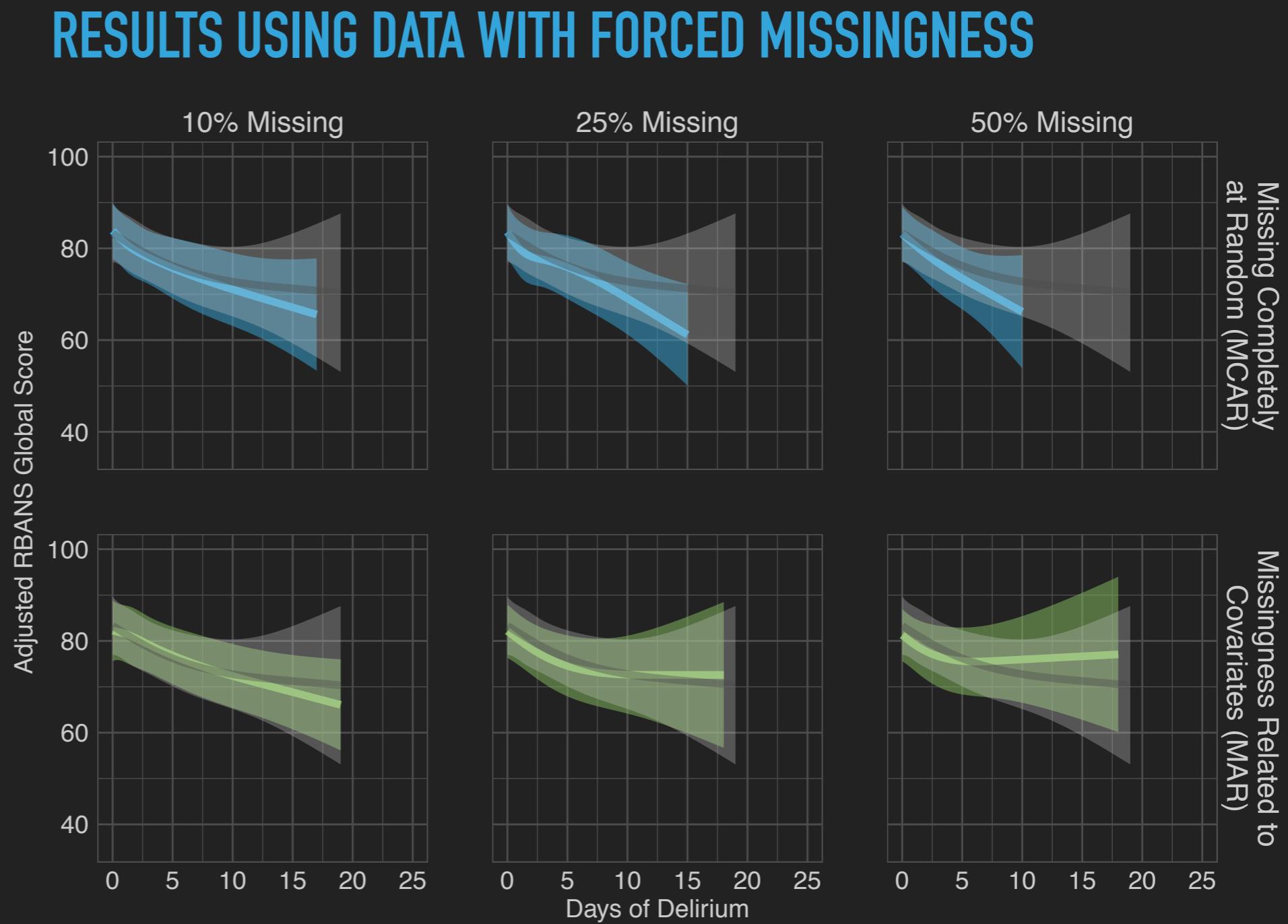
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Grayscale = original study results; color = modified as noted



THAT'S NOT GREAT... SO
WHAT ARE
MY OPTIONS?

TECHNIQUES TO HANDLE MISSING DATA

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- ▶ CONS

- ▶ Can lead to biased, misleading results
- ▶ Reduces sample size and therefore power (see [TBI example](#))

2. SINGLE IMPUTATION: MAKE AN ASSUMPTION

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Make assumption(s) about values for missing assessments, then proceed with analysis.

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- ▶ Doesn't account for uncertainty surrounding our assumptions

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Possible (But Not Necessarily Advised) Techniques:

- ▶ Assume all missing assessments are normal/delirious/coma
- ▶ Use a little clinical info:
 - ▶ LOCF
 - ▶ Missing among survivors = normal; missing among deceased = coma
- ▶ BRAIN-ICU approach: impute status based on the days before & after missing assessment

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- ▶ More complicated
- ▶ Depends on predictors being as/more reliable than delirium assessments
- ▶ Assumes assessments are **missing at random**

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BUT WAIT... ISN'T IMPUTATION MAKING UP DATA?

In a word: no.

"The goal of imputation is to preserve the information and meaning of the non-missing data." - Frank Harrell

Ignoring missing data is more of a disservice to patients and to science than addressing the resulting bias head-on.

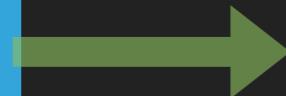
SUMMARY

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DO I HAVE <3-5%
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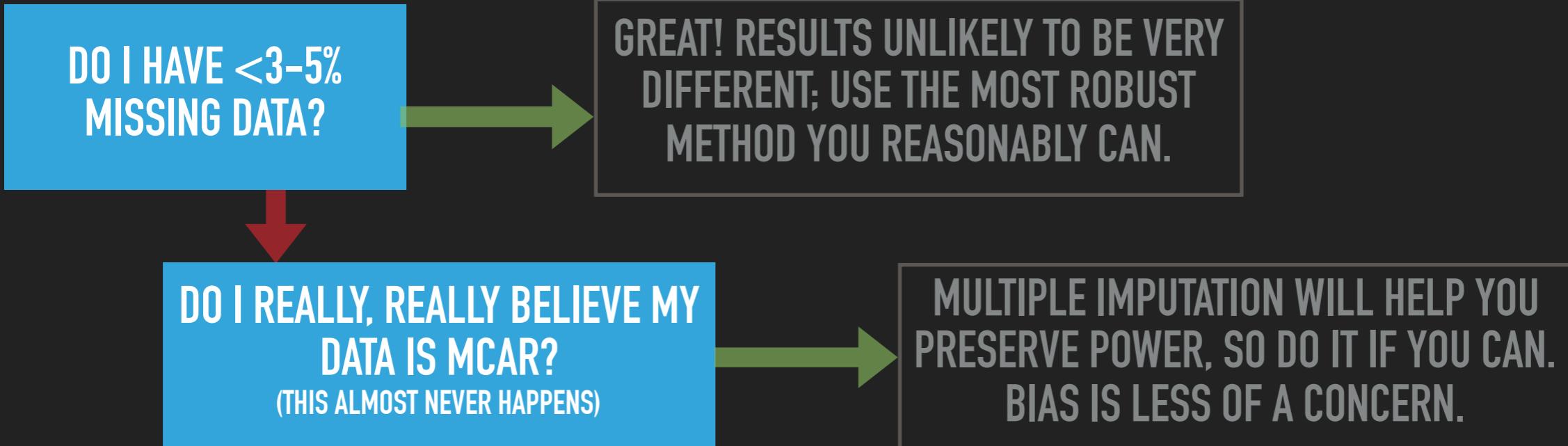
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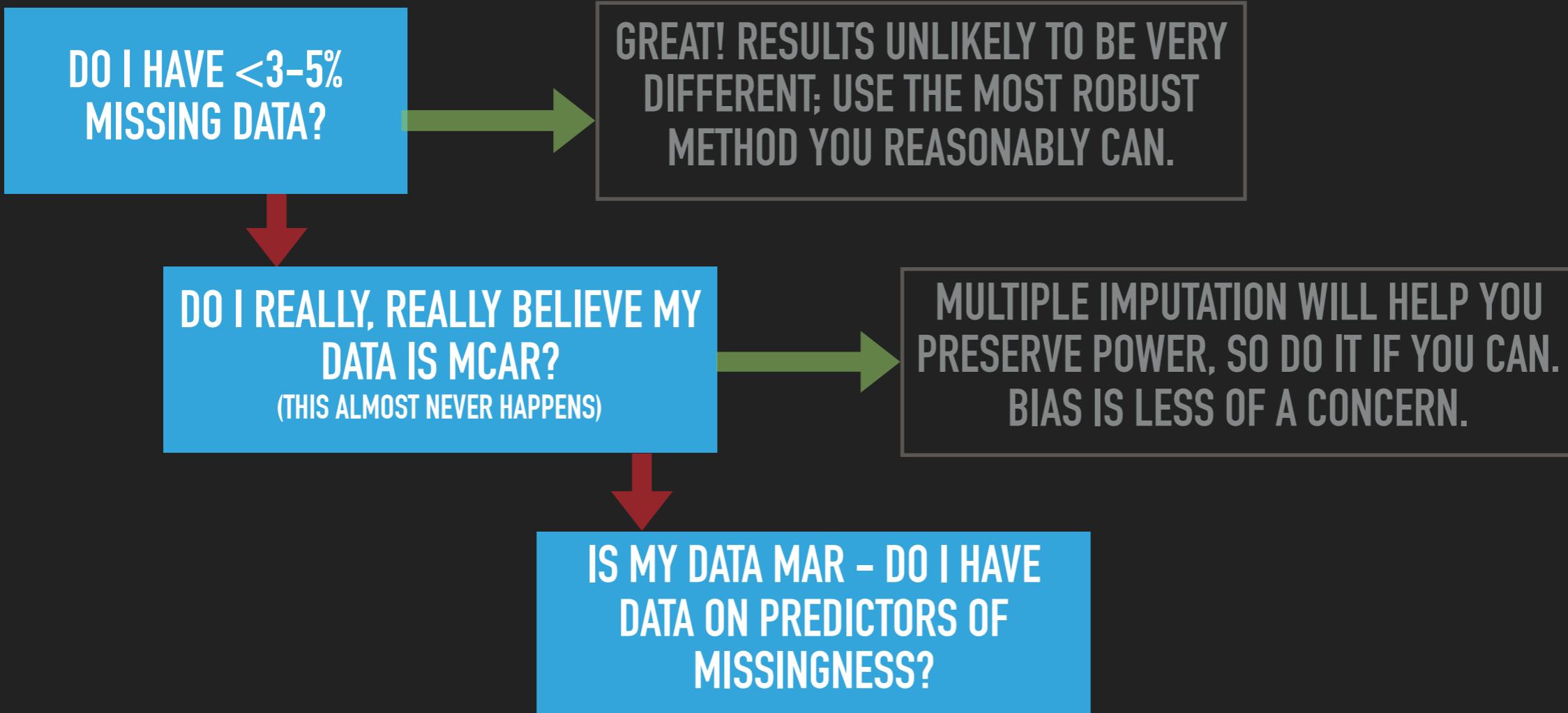
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MULTIPLE IMPUTATION WILL HELP YOU
PRESERVE POWER, SO DO IT IF YOU CAN.
BIAS IS LESS OF A CONCERN.

SAD. MAKE SURE YOU
CONSIDER POTENTIAL FOR
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IF YOU HAVE STRONG RATIONALE, DO THE BEST
SINGLE IMPUTATION AVAILABLE IN YOUR CONTEXT TO AVOID LOSING N.
MAKE SURE TO CONSIDER POTENTIAL FOR BIAS DURING INTERPRETATION.

SUMMARY

RESOURCES

- ▶ Janssen et al. "Missing covariate data in medical research: To impute is better than to ignore." *Journal of Clinical Epidemiology*, 2010 Jul;63(7):721-7. DOI: [10.1016/j.jclinepi.2009.12.008](https://doi.org/10.1016/j.jclinepi.2009.12.008)
- ▶ Donders et al. "Review: A gentle introduction to the imputation of missing values." *Journal of Clinical Epidemiology*, 2006 Oct;59(10):1087-91. DOI: [10.1016/j.jclinepi.2006.01.014](https://doi.org/10.1016/j.jclinepi.2006.01.014)
- ▶ Sterne et al. "Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls." *The BMJ*, 2009;338:b2393. DOI: [10.1136/bmj.b2393](https://doi.org/10.1136/bmj.b2393)
- ▶ Multiple imputation software options:
 - ▶ R: mice package by Stef van Buuren ([package manual](#))
 - ▶ R: Hmisc::aregImpute() by Frank Harrell ([documentation](#)), usually used in conjunction with rms::fit.mult.impute()
 - ▶ Stata: mi ([feature page](#))
 - ▶ SAS: PROC MI ([user guide](#))
- ▶ Slides (and R code for visuals, if you're really into it):
github.com/jenniferthompson/ADS2017



Jennifer Thompson @jent103 · Jun 2
On Slack, chatting with your boss about missing data on a Friday night because you both know how to party.

E. Ariño de la Rubia @earino

Following

Replying to @jent103
Ain't no party I ke a mis in dat part be ause a missi g da a party don't top.

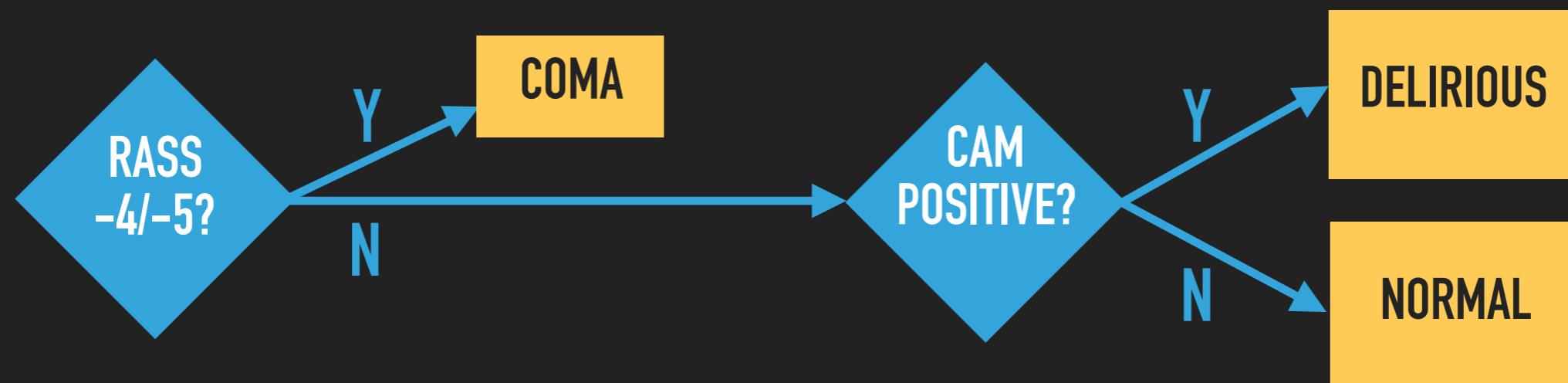
LIKES 4

10:52 PM - 2 Jun 2017

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EXAMPLE: TRAUMATIC BRAIN INJURY COHORT

Why do we need the RASS **and** the CAM-ICU for a complete assessment?



EXAMPLE: TRAUMATIC BRAIN INJURY COHORT

7% of our 2,664 patients had **no mental status assessments**.

They are **older and less injured** than the 93% who were assessed at least once.

Specifically, they:



Are **more** likely to:

- ▶ Have public insurance (46% vs 34%)
- ▶ Have full motor response (94% vs 49%) & both pupils reactive (94% vs 81%) at admission

Are **less** likely to:

- ▶ Be discharged to rehab (8% vs 24%)
- ▶ Die during hospitalization (6% vs 21%)

SUPPLEMENTARY SLIDES

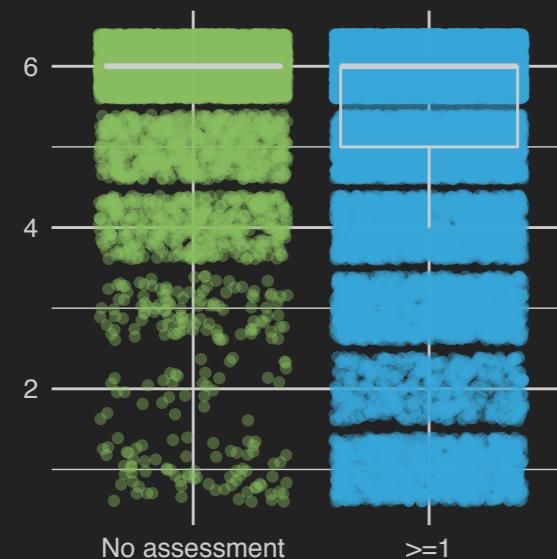
EXAMPLE: TRAUMATIC BRAIN INJURY COHORT

26% of our 31,072 patient-days had **no mental status assessments**.

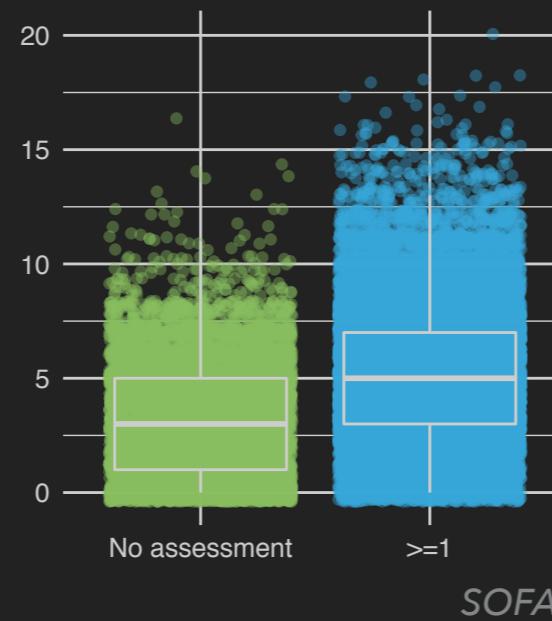
These patient-days were “better” than patients with an assessment.

Specifically, they:

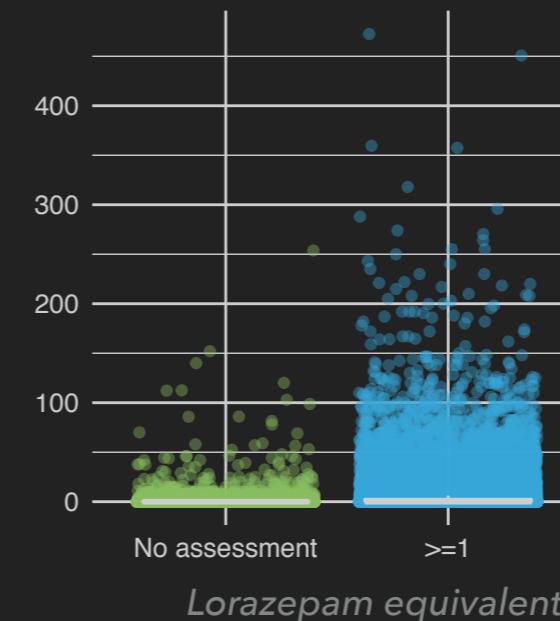
**Have better
motor response**



**Have less
organ dysfunction**



Have less **sedation
via benzodiazepines**



Have less **analgesia
via opioids**

