SUPPLEMENTAL APPENDIX

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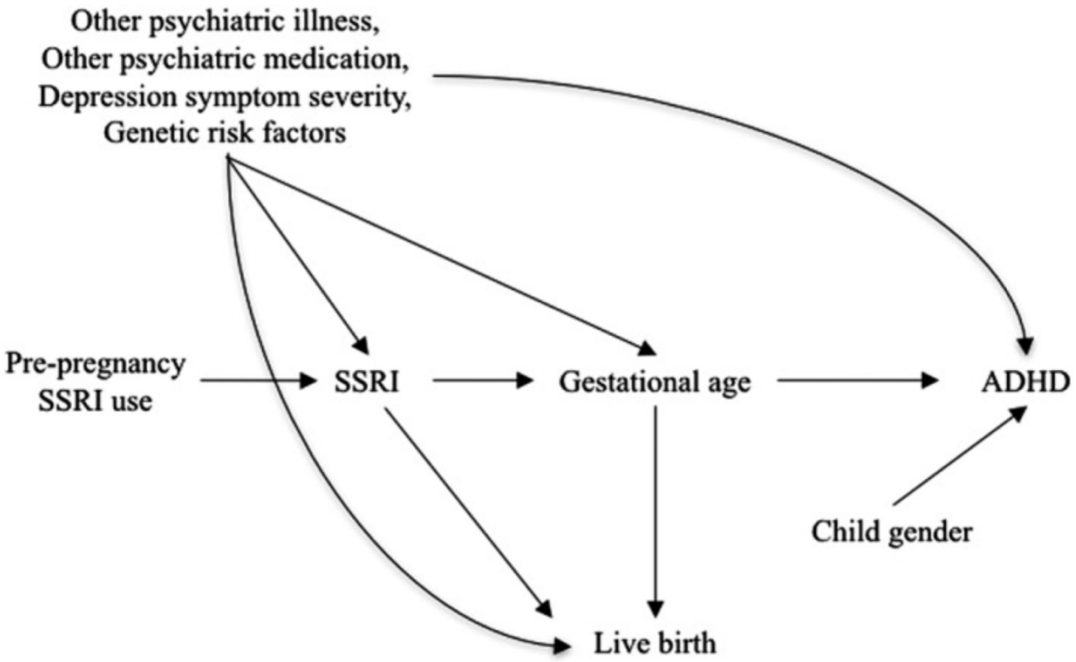


Figure S1A. Directed Acyclic Graphic (DAG) Example for Pregnancy Medication and Childhood Neurodevelopment. DAG for prenatal selective serotonin reuptake inhibitor (SSRI) medication (exposure) and attention deficit/hyperactivity disorder (ADHD) (outcome) showing potential confounders such other psychiatric illness as well as other factors including gestational age (mediator) and live birth (collier).

Source: Wood ME, Lapane KL, van Gelder MMHJ, Rai D, Nordeng HME. Making fair comparisons in pregnancy medication safety studies: An overview of advanced methods for confounding control. Pharmacoepidemiol Drug Saf. 2018 Feb;27(2):140-147. doi: 10.1002/pds.4336

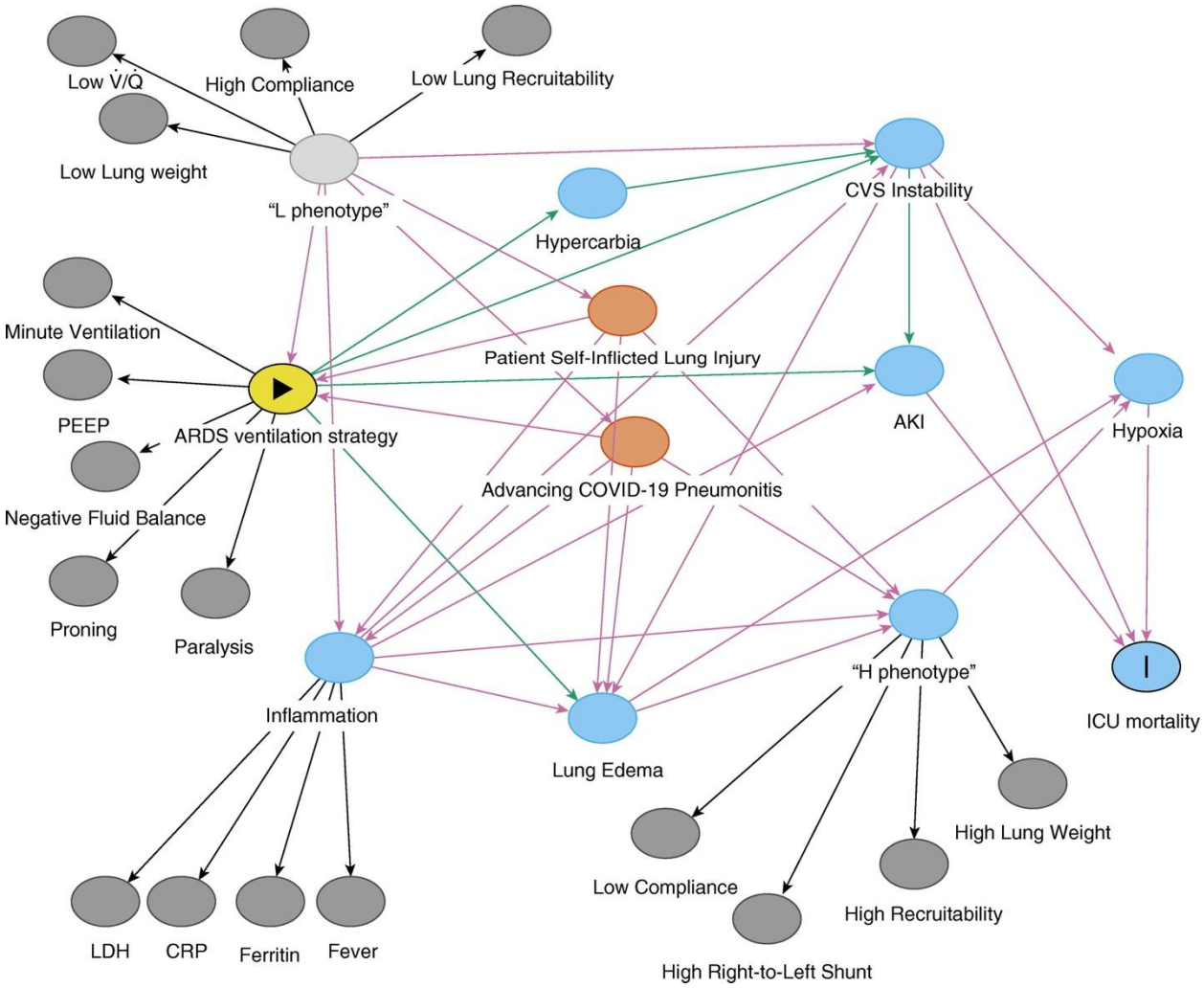


Figure S1B. Directed Acyclic Graphic (DAG) for COVID-19 ARDS Ventilation Strategy and ICU Mortality. DAG for COVID-19 acute respiratory distress syndrome (ARDS) ventilation strategy (exposure shown as yellow oval) and intensive care unit (ICU) mortality (outcome shown as blue oval with black outline and "I").

Cite: Fowler AJ, Wan YI, Carenzo L, Haines RW. COVID-19 Phenotypes and Potential Harm of Conventional Treatments: How to Prove the Hypothesis. Am J Respir Crit Care Med. 2020 Aug 15;202(4):619-621. doi: 10.1164/rccm.202004-1293LE.
The American Journal of Respiratory and Critical Care Medicine is an official journal of the American Thoracic Society.

Study characteristics and considerations		Data source #1	Data source #2	Data source #13
DESIGN ELEMENTS				
Study population	• At least 5,000 hospitalized COVID-19 patients (inpatient/hospitalization data) • Lab results to identify additional COVID-19 patients • Inpatient data linked with outpatient data • Near complete age, sex, region data	4	3	3
Treatment/exposure and comparator group(s)	• Day-level prescription data	5	5	5
Primary outcomes	• Inpatient mortality	4	1	4
Length and frequency of follow-up	• 28 days minimum • Frequency of data refresh	4	3	3
Confounding variables	• Day-level outpatient and inpatient diagnosis data	4	3	3
Key subgroups	• Day-level procedure data (mWHO COVID severity)	3	4	4
DATA ACCESS CONSIDERATIONS				
Timeline	• Time to fully executed contract • Time to data access • Time to analyze	Fast	Moderate	Slow
Contracting logistics	• Time to fully execute contract	Low	Medium	High
FINAL DATA SOURCE SELECTION		✓		

LEGEND

5 = Many/nearly all data requirements met
4 = Several data requirements met
3 = Likely that several data requirements are met but requires further investigation
2 = Some data requirements met or unable to assess at this time
1 = Data requirements not met

Figure S2. Fit-for-purpose data heatmap.

Source: Gatto NM, Campbell UB, Rubinstein E, Jaksa A, Mattox P, Mo J, Reynolds RF. The Structured Process to Identify Fit-For-Purpose Data: A Data Feasibility Assessment Framework. Clin Pharmacol Ther. 2022 Jan;111(1):122-134. doi: 10.1002/cpt.2466.

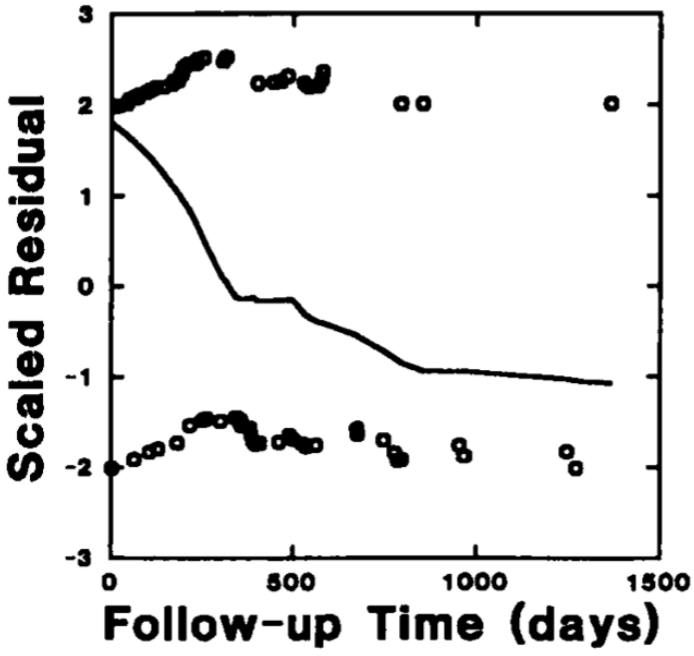


Figure S3. Plot of Schoenfeld residuals.

Source: Hess KR. Graphical methods for assessing violations of the proportional hazards assumption in Cox regression. Stat Med. 1995 Aug 15;14(15):1707-23. doi: 10.1002/sim.4780141510.

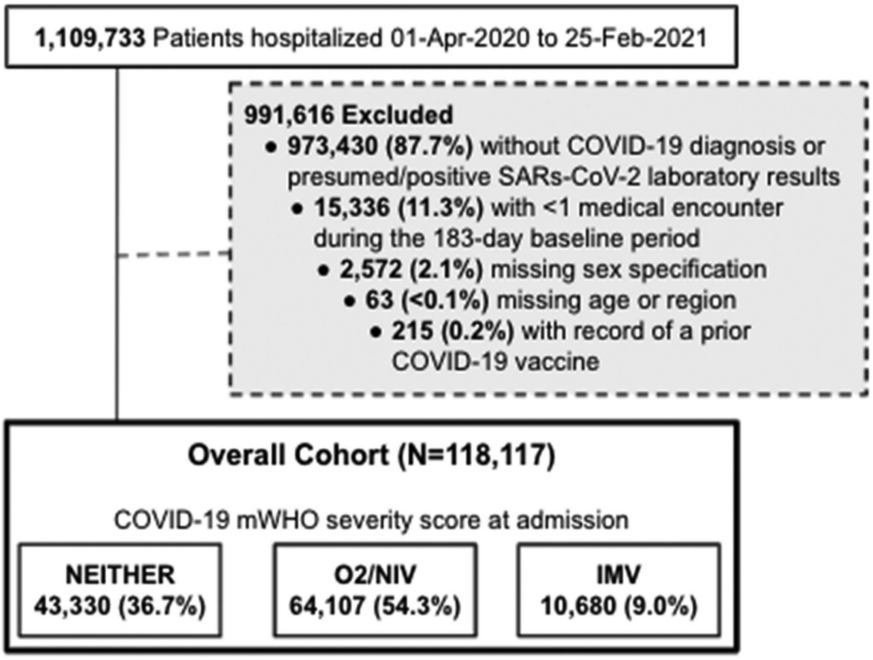


Figure S4. CONSORT flow chart.

Source: Garry EM, Weckstein AR, Quinto K, Bradley MC, Lasky T, Chakravarty A, Leonard S, Vititoe SE, Easthausen IJ, Rassen JA, Gatto NM. Categorization of COVID-19 severity to determine mortality risk. Pharmacoepidemiol Drug Saf. 2022 Apr 4. doi: 10.1002/pds.5436. Epub ahead of print.

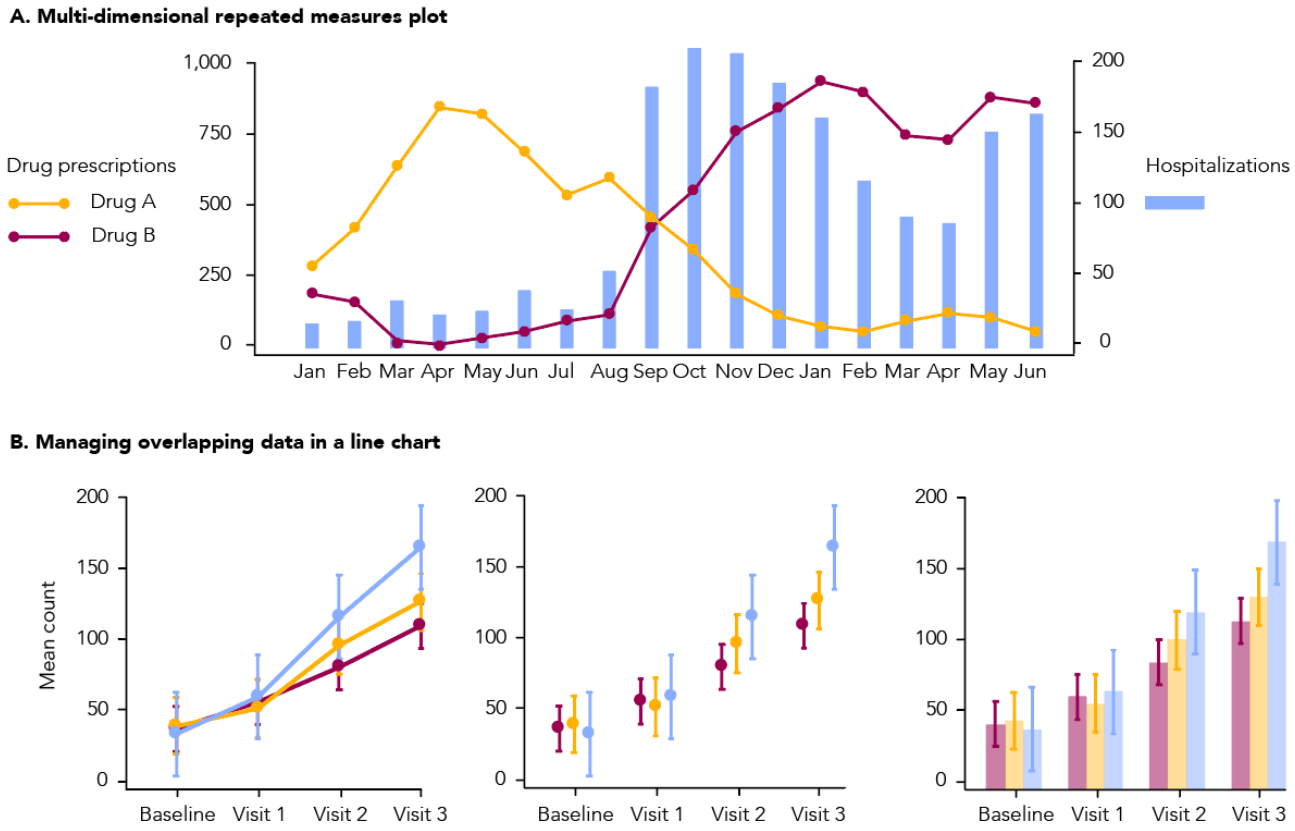


Figure S5. Repeated measures plots.

(**A**): A plot with multiple dimensions (number of drug prescriptions and number of hospitalizations), with different visualization types (line charts and bar charts) representing the different dimensions to aid understanding. (**B**) The line chart on the far left illustrates overlapping data, where it is difficult to discern differences between groups. The two plots on the right show possible solutions to address this problem.

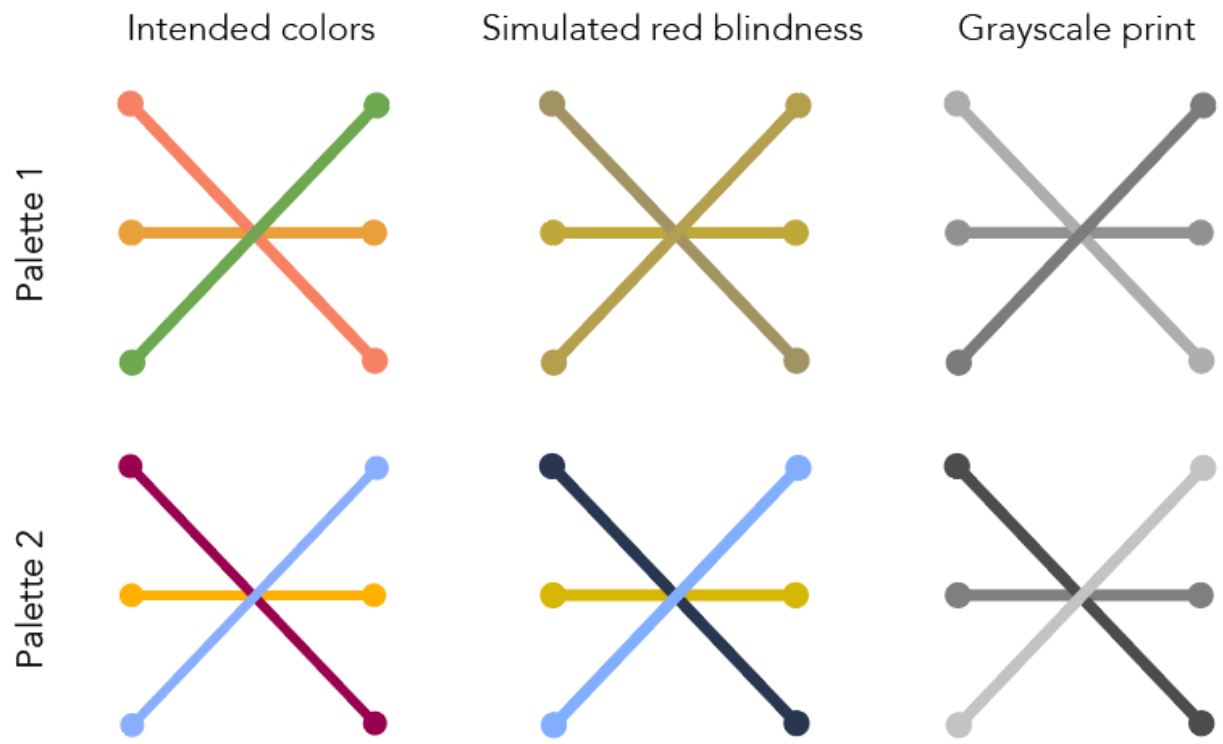
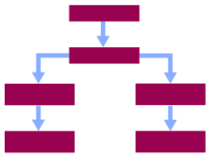
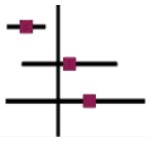


Figure S6. Palette choice vs. color blindness and grayscale printing.

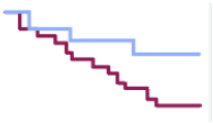
Colors should be selected to ensure optimal accessibility of a plot, with consideration given to color blindness and the possibility that the plot may be printed in gray scale. Palette 1 demonstrates sub-optimal color choices, whereas palette 2 demonstrates better preservation of underlying group differences under simulated red blindness and grayscale printing.

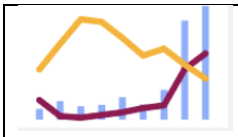
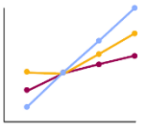
Table S1. Recommendations for visualization of results

Visualization type	Recommendations
Cohort attrition: flow diagrams 	• For database studies, top-line numbers should indicate the total number of patients available in the database. If the study involved database linkage, then the data linkage should be illustrated, including the total number of patients in each contributing dataset, and the number of patients with linked data. • Use descriptive labels if concise and helpful to the reader. For example, rather than generic labels such as "Treatment arm" and "Comparator arm", consider study-specific labels such as "Prasgurel (treatment arm)" and "Clopidogrel (comparator arm"). • Every exclusion criterion should be listed, together with the number of patients meeting each criterion. As exclusion criteria are typically imposed sequentially, each excluded patient should only meet a single exclusion criterion. • Once patients are divided into groups (e.g., assigned to treatment groups), do not merge them together again later in the flow chart; continue to report attrition for each group separately. • Verify that all patients in the dataset are fully accounted for: the sum of all inclusion and exclusion steps should result in the final count of patients available for analysis. • If the cohort attrition is particularly complicated, such as may be the case if there are numerous treatment arms or databases involved, consider describing cohort attrition as a table rather than figure.
Effect estimates: forest plots 	• Effect estimates expressed as ratios (e.g., odds ratios and hazard ratios) should be displayed on the horizontal axis using a logarithmic scale.[1,2] This allows inverse numbers that have equal strengths of association (e.g., odds ratios of 2 and 0.5) to be visually equidistant from 1. If a linear scale were used to illustrate ratios, then it may be more difficult to interpret confidence intervals, as their upper and lower bounds will be asymmetric around the point estimate. In contrast, linear effect estimates (e.g., absolute differences or incidence rates) should be displayed using a linear scale. • To aid interpretation of the horizontal axis, label the directions of effect on either side of null with the comparison group that is favored (e.g., "Favors prasgurel" or "Favors clopidogrel").

[1] Pocock SJ, Travison TG, Wruck LM. How to interpret figures in reports of clinical trials. BMJ. 2008 May 24;336(7654):1166-9. doi: 10.1136/bmj.39561.548924.94. PMID: 18497415; PMCID: PMC2394578.

[2] Cruz-Retamozo X, Prado-Ghezzi D, Pereyra-Elías R. Forest Plots: Linear or Logarithmic Scale? J Adolesc Health. 2017 Nov;61(5):664-665. doi: 10.1016/j.jadohealth.2017.07.025. PMID: 29061236.

	• Provide numerical point estimates, confidence intervals, sample sizes, and event counts (if applicable) in tabular format adjacent to the forest plot. If a pooled estimate is being reported, also include the percentage weight contribution of each individual estimate to the pooled estimate. • Consider illustrating additional descriptive information adjacent to the forest plot if it provides key information that can help the reader understand differences between estimates. For example, if different estimates pertain to different levels of adjustment in a regression model, those changes in the regression model can be depicted next to the forest plot (**Figure 5**). • Consider truncating unusually large confidence intervals if doing so allows better interpretation of other results. Arrow heads can be used to indicate truncated intervals. • If the plot contains many rows and columns, consider providing background shading on alternating lines to make it easier for the eye to follow information horizontally across the table.
Time-to-event analysis: Kaplan-Meier plots 	• Careful consideration should be made to the design of the vertical axis, as this can impact the visual perception of overall survival and differences between groups. For example, if the vertical axis for survival only extends part way through the probability range (e.g., 1.0 to 0.9), this could deceptively exaggerate decreases in survival over time (**Figure 6**). Therefore, in most cases, vertical axes for survival probability should range from 1.0 to 0.0. On the other hand, if events are rare, it may be difficult to see changes in probability or differences between groups in such survival plots. In such cases, it may be preferable to display data as a cumulative incidence rather than survival. • Confidence intervals or other representations of uncertainty should be displayed, unless they unduly complicate the plot. • Number of patients at risk (those still in follow-up and who have not yet experienced the outcome) at selected time points should be tabulated below the horizontal axis. This can help the reader interpret how the sample size changes over time. • Summary point estimates (e.g., hazard ratios) with confidence intervals should be included directly in the plot, to aid interpretation of statistical differences between curves.
Repeated measures: line charts, bar charts, and box plots	• Line charts are typically the preferred chart type for visualizing repeated measures, as data trends can be easy to perceive. In addition, they may be suitable for representing multiple dimensions of data to illustrate joint trends over time (**Figure S5A**). • Line charts may be less ideal in data with many overlapping lines, which can obscure trends (**Figure S5B**). Such cases may be addressed by offsetting points from one another on the horizontal axis, by not joining

	points with lines, by using bar charts, or simply reporting the data in tabular format. • For line charts, data points should be indicated with a symbol (e.g., a circle, square, or diamond), as without this it can be difficult to determine what is an observation and what is an interpolation. • Box plots may be considered when it is important to capture the shape of the distribution for numerical values, which may be relevant for highly non-normally distributed data such as resource utilization. Lines may be drawn between central estimates (e.g., medians) to better visualize overall trends in such cases. • Error bars (e.g., capturing standard deviation, confidence intervals, or other measures of uncertainty) should generally be shown.
Change of state: Sankey diagram 	• Consider labeling each node with its number of corresponding patients, so that precise numerical values can be drawn from the data (**Figure 7A**). • If appropriate, arrange nodes from top to bottom along a conceptual hierarchy, such as disease severity or therapy line number, as this can aid interpretation of the plot. • Losses to follow-up and other types of missing data should be handled with appropriate methods for censored data. • As data complexity increases, Sankey plots becomes more difficult to interpret. Consider simplifying the data in such cases, such as collapsing conceptually similar nodes together into one category. • Sankey plots can also be simplified by focusing on a particular node, such as by visually highlighting on those paths originating from a particular initial node (e.g., first line of therapy; **Figure 7B**), or only highlighting paths that ascend in hierarchy (e.g., increasingly severe disease state).
General style 	• Select the plot type that makes data trends and comparisons most apparent. For example, when proportions are reported, pie charts should be able to avoid as visual comparison of group sizes can be difficult, whereas bar charts allow such comparison more readily. • Avoid lines, borders, or shading that do not contribute to understanding of a figure, as this can add complexity without benefit (**Figure 8A**). • Redundant or superfluous information should be removed. For example, when labeling figures, remove percentage symbols on every tick mark label and instead place it on the axis label (**Figure 8B**). Additionally, keep axis tick marks to a minimum unless they are key to understanding the plot (**Figure 8B**). • Consider eliminating unnecessary space between figure elements, such as broad distances between rows and columns in a chart, or unnecessarily broad axis ranges (**Figure 8C and 8D**).

	● Consider accessibility when selecting colors (**Figure S6**).[3] For example, choose a palette that is color blind friendly. In general, this means avoiding the use of red in combination with green, although other types of color blindness must be considered as well. Tools exist that can be used to help select color blind-friendly colors or simulate illustrations under different types of color blindness.[3] Moreover, consider how the figure looks in greyscale by desaturating it, as some colors may appear indistinct when the figure is printed in black and white. ● If numerical values used to generate a plot are not directly provided in text on the figure (e.g., a bar chart illustrating mean costs, but where the specific values of the costs are not directly listed) or in the main manuscript, consider providing them in an appendix to the paper. This can help readers cite specific information, such as may be important for including the study in future meta-analyses.

[3] Katsnelson A. Colour me better: fixing figures for colour blindness. Nature. 2021 Oct;598(7879):224-225. doi: 10.1038/d41586-021-02696-z. PMID: 34608306.