Research Letter

TWISTER PLOTS FOR TIME-TO-EVENT STUDIES

Results of randomized trials and observational studies can be difficult to communicate. Results are often presented as risk or survival functions stratified by the treatment or exposure (1, 2). However, a contrast between the stratified risk functions is often of primary interest. Here we propose a "twister" plot to visualize contrasts in risk over the duration of a study. The twister plot is a −90-degree rotation of a typical contrast measure plot (e.g., Figure 3 in Cole et al. (3)), whereby the contrast measure is instead on the abscissa (*x*-axis) and time on the ordinate (*y*-axis). Pointwise confidence intervals are similarly added as a shaded region that typically widens as follow-up duration increases, giving twister plots their characteristic shape that resembles their namesake. To ease application, we provide SAS, R, and Python code on GitHub (4).

In Figure 1A, we showcase the proposed twister plot using the recent phase 3 trial results from the Pfizer BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine (1). Because individual-level COVID-19 incidence times are not publicly available, we constructed a data set from the reported number of events and censoring. In Figure 13 of the *Pfizer-BioNTech COVID-19 Vaccine (BNT162, PF-07302048) Vaccines and Related Biological Products Advisory Committee Briefing Document* (5), the number of events and number at risk are reported every 7 days from the first dose of vaccine or placebo. For each period, pseudodata were constructed from the number of events in that period for each trial arm (vaccine vs. placebo). Event times were drawn from a uniform distribution for each 7-day period. The same process was repeated to generate censoring times. The pseudodata construction process resulted in a data set with the same number of events and censored observations per 7-day period. To estimate the risk function for each trial arm, we used the complement of the Kaplan–Meier estimator (6). Standard errors for the risk were estimated using Greenwood's formula (7). Standard errors for the estimated risk difference were estimated using a linear combination of the standard errors of the risks. Although demonstrated for the risk difference, the twister plot can be readily applied to other contrast measures, such as risk ratios (Web Figure 1,
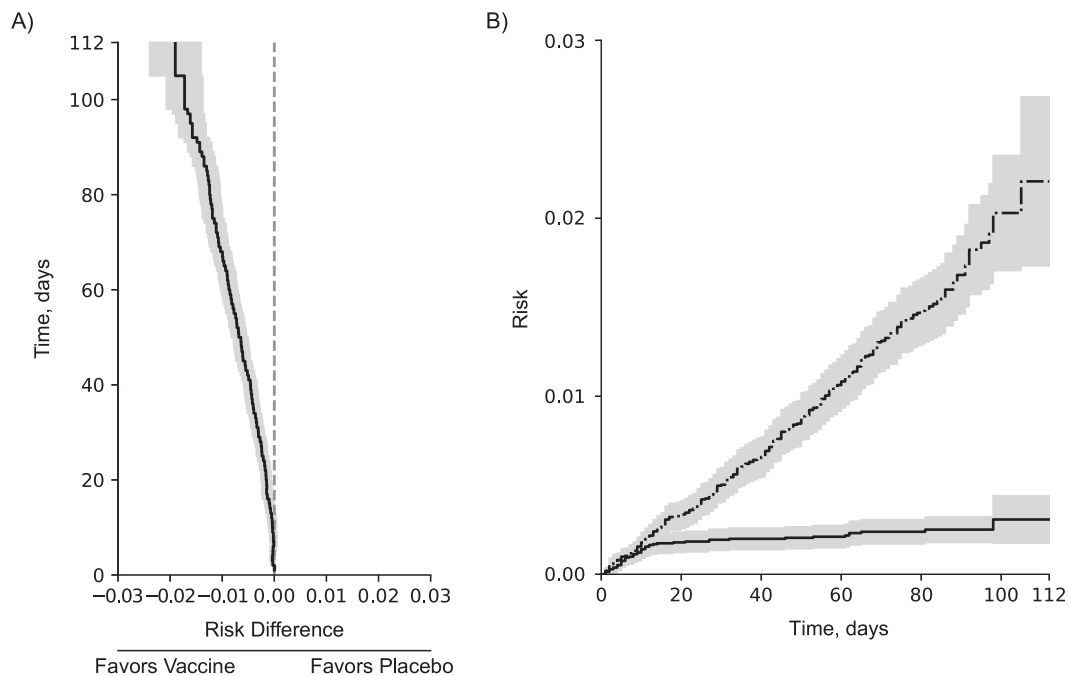

Figure 1. Twister plot (A) and risk curves (B) for the Pfizer BNT162b2 vaccine and placebo over days from first dose. A) Twister plot of the risk difference over follow-up. B) Risk functions stratified by vaccination status over follow-up. Dashed line indicates the placebo arm; shaded regions indicate 95% confidence intervals. Event and censoring times were reconstructed from published interval data from the BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine phase 3 trial. Risks were estimated using the complement of the Kaplan–Meier estimator, stratified by trial arm. Standard errors for the risks were estimated using Greenwood's formula (7). Risk differences were calculated via the risk in the vaccine arm minus the risk in the placebo arm. Standard errors for the estimated risk difference were estimated using a linear combination of the standard errors of the risks. "Favors vaccine" indicates a lower risk of COVID-19 or severe COVID-19 among the vaccine arm compared to placebo.

available at https://doi.org/10.1093/aje/kwab231). An advantage of twister plots is the ability to clearly label the favored space for each treatment or exposure, as with forest plots, and visualize the confidence intervals for the parameter of interest (compared with Figure 1B). The central result of beneficial effect of the vaccine is demonstrated using the twister plot, and use of twister plots may enhance communication of results.

REFERENCES

1. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med.* 2020; 383(27):2603–2615.
2. Baden LR, el Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* 2021; 384(5):403–416.
3. Cole SR, Lau B, Eron JJ, et al. Estimation of the standardized risk difference and ratio in a competing risks framework: application to injection drug use and progression to AIDS after initiation of antiretroviral therapy. *Am J Epidemiol.* 2015; 181(4):238–245.
4. Zivich P. Publications code. https://github.com/pzivich/publications-code. Published August 23, 2021. Accessed August 23, 2021.
5. Pfizer-BioNTech. *Pfizer-BioNTech COVID-19 Vaccine (BNT162, PF-07302048) Vaccines and Related Biological Products Advisory Committee Briefing Document*. Silver Spring, MD: US Food and Drug Administration; 2020. https://www.fda.gov/media/144246/download. Accessed August 20, 2021.
6. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc.* 1958;53(282): 457–481.
7. Greenwood M. The natural duration of cancer. In: *Reports on Public Health and Medical Subjects*. Vol. 33. London, UK: Her Majesty's Stationery Office; 1926:1–26.

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